

REMARKS

Upon entry of the foregoing amendments, allowed claims 33, 34 and 49-52, and currently rejected claims 53-58 will be pending in the application. Claims 33, 53 and 56 are independent claims.

Independent claims 53 and 56 have been amended to more particularly point out and distinctly claim the subject matter which Applicants regard as their rejection. The amendments recite that the isolated protein of each claim is not a full length NhhA polypeptide. This is supported by the application as originally filed. The invention has always excluded full length NhhA polypeptides. See, for example, page 3, lines 1-6. These claims have also been amended to use the proper italics for the microorganism *N. meningitides*. Since no new matter has been added by the amendments, their entry is respectfully solicited.

Applicants traverse the rejection of claims 53-59 for the following reasons.

35 USC §112, First Paragraph - Enablement

The Examiner has stated at page 7 of the Office Action that claims 53-58 do not comply with section 112, first paragraph, reiterating that this is an enablement rejection. The Examiner has asserted, in essence summarizing this rejection: "Applicant has shown how to make and use SEQ ID NOS:23 and 35 but has not shown how to make variants of the polypeptides as set forth in SEQ ID NOS:23 and 35 that retain the same functional properties." [Original emphasis].

With respect, the specification has always provided variants of these sequences and how to make and use them.

The following tables show the level of sequence identity between SEQ ID NOS:23 and 35 and other isolated proteins set forth in the specification as originally filed. The comparisons are based on ClustalW (v. 1.4) program sequence alignments, within the MacVector sequence analysis package. Copies of the printouts on which the tables are based are submitted with this Amendment.

Comparison	% identity
------------	---------------

SEQ ID NO: 23 vs 24	95
SEQ ID NO: 23 vs 25	79
SEQ ID NO: 23 vs 26	84
SEQ ID NO: 23 vs 27	93
SEQ ID NO: 23 vs 35	90
SEQ ID NO: 23 vs 36	85
SEQ ID NO: 23 vs 37	69
SEQ ID NO: 23 vs 38	74
SEQ ID NO: 23 vs 39	84

Comparison	% identity
SEQ ID NO: 35 vs 23	90
SEQ ID NO: 35 vs 24	85
SEQ ID NO: 35 vs 25	79
SEQ ID NO: 35 vs 26	93
SEQ ID NO: 35 vs 27	85
SEQ ID NO: 35 vs 36	95
SEQ ID NO: 35 vs 37	77
SEQ ID NO: 35 vs 38	82
SEQ ID NO: 35 vs 39	93

Applicants submit that the high level of sequence identity between many of these sequences (generally 79%-95%) support the levels of identity recited by claims 53 and 56. These are all proteins engineered to provide cross-strain immunity to *N. meningitidis*. They all share a deletion of most or all of the V1 region and in some cases, deletion of other V regions. Thus, Applicants respectfully contend that they fall squarely within the ambit of “variants,” in the words of the Examiner. Therefore, Applicants submit that they have indeed provided a representative number of species within the claimed genus of polypeptides and, accordingly, that we have shown how to make variants of the polypeptides as set forth in SEQ ID NOS:23 and 35.

Also at page 7 of the Office Action, the Examiner has commented on Figure 1 and Table 1 of the specification as “merely disclosing conserved regions and variable regions...which are used to generate a consensus sequence.... Figure 1 and Table 1 in no way convey which amino acids are modified....”

With respect, while Table 1 indeed discloses conserved and variable regions, claims 23 and 35 are not predicated on, or restricted to, isolated proteins which are modified by amino acid sequence modification (*e.g.* by substitution). A very large number of protein sequences having at least 80% or 90% sequence identity to SEQ ID NO:23 or 35 can be made by replacing, deleting and/or shuffling V and/or C regions, with a view to creating a protein that elicits a more cross-protective immune response. This is a process well within the capabilities of a person of ordinary skill in the art armed with Table 1.

Notwithstanding this ability, Figure 1 indeed shows which modifications to make to thereby ensure that a protein can be made that is less strain-specific or more cross-protective.

Figure 1 indicates residue-by-residue, for each of SEQ ID NOS:1-10, the variations that can occur. This information can be readily applied to SEQ ID NO:23 and SEQ ID NO:35, because these sequences are derived from SEQ ID NO: 1.

In some cases, residues are absolutely conserved between SEQ ID NOS:1-10 (*e.g.* residue 62 L); in some cases, a limited set of variations occurs between SEQ ID NOS:1-10 (*e.g.* residue 72 G or L); in some cases, a more extensive set of variations occurs between SEQ ID NOS:1-10 (*e.g.* residue 106 G, R, A or I); and in some cases certain residues may be present or absent between SEQ ID NOS:1-10 (*e.g.* residue 57 may be E or entirely absent).

This requires no guesswork or undue experimentation. The variations are all spelled out in FIG. 1.

This is very useful guidance to enable a skilled person to decide which amino acids of SEQ ID NO:23 or SEQ ID NO:35 can be deleted (*e.g.* residues that vary considerably between SEQ ID NOS:1-10 or are not always present in SEQ ID NOS:1-10) to maximize cross-protection. Furthermore, Figure 1 allows the identification of modifications that retain relatively invariant residues, or substitutions of an amino acid residue with another residue that is typically present in one or more of SEQ ID NOS:1-10, to thereby maximize cross-protection.

In summary, the specification provides more than an adequate representative number of species of the genus of proteins encompassed by claims 53-58. Furthermore, sufficient, explicit guidance is provided by Table 1, Figure 1 and the specification in general to readily enable a skilled

person to make amino acid sequence modifications that fall within the ambit of claims 53-58. The variants clearly would be used in substantially the same way as SEQ ID NOS:23 and 35.

Applicants therefore submit that the enablement rejection of claims 53-58 as currently amended is no appropriate. Favorable reconsideration and withdrawal of these rejections are respectfully solicited.

35 USC §102 (a) - Novelty

Masignani

The Examiner has cited Masignani as disclosing a protein sequence (SEQ ID NO:4 of Masignani) that allegedly has over 98% identity to SEQ ID NO: 23 and at least 98% sequence identity to SEQ ID NO:35.

Applicants submit that claims 53-58 are *prima facie* novel over Masignani by virtue of the recitation in claims 53 and 56 that the isolated protein is not a full length NhhA polypeptide. In contrast, SEQ ID NO:4 of Masignani is a full length NhhA polypeptide.

Applicants respectfully question how the Examiner arrived at the alleged levels of identity specified in this rejection, as their own analysis reveals substantially less identity.

Claims 53 and 56 recite that the at least 80% or 90% identity is compared across the entire length of the protein relative to SEQ ID NOS:35 or 23, respectively.

SEQ ID NO:23 has a deletion (compared to the full length NhhA polypeptide of SEQ ID NO:1) of residues 55-133 (see Example 4). SEQ ID NO:1 is the same sequence as SEQ ID NO:4 of Masignani. This is a significant deletion.

A ClustalW comparison of SEQ ID NO:23 with SEQ ID NO:4 of Masignani reveals only about 86% identity over the entire sequences. A copy of a printout based on this comparison is enclosed with this Amendment. This clearly is outside the scope of claim 56, and further distinguishes the subject matter of claims 56-58 from Masignani.

SEQ ID NO:35 has a further 51 amino acid deletion (compared to the full length NhhA polypeptide of SEQ ID NO:1) due to N-terminal processing (see Example 4).

A ClustalW comparison of SEQ ID NO:35 with SEQ ID NO:4 of Masignani reveals only 77% identity over the entire sequences. A printout of the analysis is enclosed with this Amendment. This is outside the scope of both of claims 53-58, and further distinguishes the claimed proteins from Masignani.

In view of the data presented with the enclosures to this Amendment, Applicants cannot understand how the 98% level of identity with Massignani is arrived at by the Examiner.

Nevertheless, as pointed out above, the sequences encompassed by claims 53-58 are not full length NhhA polypeptides, such as SEQ ID NO:4 of Massignani and exclude from their scope sequences such as SEQ ID NO:4 of Massignani.

Peak

The Examiner has cited Peak as disclosing a protein sequence (SEQ ID NO:2 of Peak) that allegedly has over 98% identity to SEQ ID NO: 23 and at least 99% sequence identity to SEQ ID NO:35.

Applicants submit that claims 53-58 are *prima facie* novel over Peak by virtue of the recitations in claims 53 and 56 that the isolated protein is not a full length NhhA polypeptide. In contrast, SEQ ID NO:2 of Peak is a full length NhhA polypeptide.

Moreover, as with Massignani, Applicants question how the Examiner arrived at the alleged levels of identity compared to Peak specified in this rejection.

Claims 53 and 56 recite that the at least 80% or 90% identity is compared across the entire length of the protein relative to SEQ ID NOS:35 or 23, respectively. SEQ ID NO:23 has a deletion (compared to the full length NhhA polypeptide of SEQ ID NO:1) of residues 55-133 (see Example 4).

SEQ ID NO:1 in the present application is 99.6% identical to SEQ ID NO:2 of Peak.

A ClustalW comparison of SEQ ID NO:23 with SEQ ID NO:2 of Peak reveals only about 86% identity over the entire sequences. A printout based on this comparison is enclosed with this Amendment. This is outside the scope of claim 56, and further distinguishes claims 56-58 from Peak.

SEQ ID NO:35 has a further 51 amino acid deletion (compared to a full length NhhA polypeptide) due to N-terminal processing (see Example 4).

A ClustalW comparison of SEQ ID NO:35 with SEQ ID NO:2 of Peak reveals only 77% identity over the entire sequences. A printout based on this comparison is enclosed with this Amendment. This is outside the scope of all of claims 53-58.

In view of the data presented with the enclosures to this Amendment, Applicants cannot understand how the 98% - 99% level of identity with Peak is arrived at by the Examiner.

Nevertheless, as pointed out above, the sequences encompassed by claims 53-58 are not full length NhhA polypeptides, such as SEQ ID NO:2 of Peak and exclude from their scope sequences such as SEQ ID NO:2 of Peak.

In view of the significant distinctions between the claimed invention on the one hand and Massignani and Peak on the other hand, Applicants respectfully submit that the novelty rejection under section 102(a) is moot and request favorable reconsideration and withdrawal of these prior art rejections. Moreover, the cited prior art would not render the subject matter of these claims obvious.


While Applicants appreciate the prior indication of allowability of claims 33, 34 and 49-52, reconsideration and withdrawal of all of the rejections of claims 53-58 and an early Notice of Allowance relating to all claims are respectfully solicited.

Respectfully submitted,

IAN RICHARD ANSELM PEAK *et al.*

December 6, 2006
(Date)

By:


ALAN S. NADEL
Registration No. 27,363
AKIN GUMP STRAUSS HAUER & FELD LLP
One Commerce Square
2005 Market Street, Suite 2200
Philadelphia, PA 19103-7013
Telephone: 215-965-1200
Direct Dial: 215-965-1280
Facsimile: 215-965-1210
E-Mail: anadel@akingump.com

ASN:hg
Enclosures

US App. 09/771,382 Alignments of SEQ ID Nos: 23-27 and 35-39

Attached are documents that provide the sequences for alignment in US App. 09/771,382.

The purpose is:

- (a) to determine the % identity between SEQ ID NO:23 and all other sequences provided in the list
- (b) to determine the % identity between SEQ ID NO:35 and all other sequences provided in the list

This includes determining the % identity between SEQ ID NO:23 and SEQ ID NO:35.

The determination should be over the entire length of each protein.

Results:

SEQ ID NO	23	24	25	26	27	35	36	37	38	39
23	100%	95%	79%	84%	93%	90%	85%	69%	74%	84%
35	90%	85%	79%	84%	85%	100%	95%	77%	82%	93%

Comparisons were done using ClustalW, within the MacVector sequence analysis package. Alignments, details of parameters used and comparisons are detailed in the attached pages.

SEQ ID NO:23

MNKIYRIIWN	SALNAWVVVS	ELTRNHTKRA	SATVKTAVLA	TLLFATVQAS	ANNETDLTSV	60
GTEKLSFSAN	GNKVNITSdT	KGLNFAKETA	GTNGDTTVHL	NGIGSTLTDT	LLNTGATTNV	120
TNDNVTDDEK	KRAASVKDVL	NAGWNIKGVK	PGTTASDNVD	FVRTYDTVEF	LSADTKTTTV	180
NVESKDNGKK	TEVKIGAKTS	VIKEKDGLV	TGKDKGENGS	STDEGEGLVT	AKEVIDAVNK	240
AGWRMKTITA	NGQTGQADKF	ETVTSGTNVT	FASGKGTTAT	VSKDDQGNIT	VMYDVNVGDA	300
LNVNQLQNSG	WNLDSKAVAG	SSGKVISGNV	SPSKGKMDT	VNINAGNNIE	ITRNGKNIDI	360
ATSMTPQFSS	VSLGAGADAP	TLSDVDGDLN	VGSKKDNKPV	RITNVAPGVK	EGDVTNVAQL	420
KGVAQNLLNR	IDNVDGNARA	GIAQAIATAG	LVQAYLPGKS	MMAIGGGTYR	GEAGYAIGYS	480
SISDGGNWII	KGTASGNSRG	HFGASASVGY	QW			

SEQ ID NO:24

MNKIYRIIWN	SALNAWVAVS	ELTRNHTKRA	SATVKTAVLA	TLLFATVQAN	ATDETGLINV	60
ETEKLSFGAN	GKKVNIISDT	KGLNFAKETA	GTNGDTTVHL	NGIGSTLTDM	LLNTGATTNV	120
TNDNVTDDEK	KRAASVKDVL	NAGWNIKGVK	PGTTASDNVD	FVRTYDTVEF	LSADTKTTTV	180
NVESKDNGKK	TEVKIGAKTS	VIKEKDGLV	TGKDKGENGS	STDEGEGLVT	AKEVIDAVNK	240
AGWRMKTITA	NGQTGQADKF	ETVTSGTKVT	FASGNGTTAT	VSKDDQGNIT	VKYDVNVGDA	300
LNVNQLQNSG	WNLDSKAVAG	SSGKVISGNV	SPSKGKMDT	VNINAGNNIE	ITRNGKNIDI	360
ATSMTPQFSS	VSLGAGADAP	TLSDVDEGAL	NVGSKDANKP	VRITNVAPGV	KEGDVTNVAQ	420
LKGVAQNLLN	RIDNVNGNAR	AGIAQAIATA	GLVQAYLPGK	SMMAIGGGTY	LGEAGYAIGY	480
SSISAGGNWI	IKGTASGNSR	GHHFGASASVG	YQW			513

SEQ ID NO:25

MNKIYRIIWN	SALNAWVVVS	ELTRNHTKRA	SATVKTAVLA	TLLFATVQAS	ANNVDFVRTY	60
DTVEFLSADT	KTTTTNVESK	DNGKKTEVKI	GAKTSVIEKE	DGKLVTGKDK	GENGSSTDEG	120
EGLVTAKEVI	DAVNKAGWRM	KTTTANGQTG	QADKFETVTS	GTNVTFASGK	GTTATVSKDD	180
QGNITVMYDV	NVGDALNVNQ	LQNSGWNLDS	KAVAGSSGKV	ISGNVSPSKG	KMDETVNINA	240
GNNIEITRNG	KNIDIATSMT	PQFSSVSLGA	GADAPTLSDV	GDALNVGSKK	DNKPVRLTNV	300
APGVKEGDVT	NVAQLKGVAQ	LLNNRIDNVD	GNARAGIAQA	IATAGLVQAY	LPGKSMMAIG	360
GGTYRGEAGY	AIGYSSISDG	GNWIIKGTAS	GNSRGHFGAS	ASVGYQW		407

SEQ ID NO:26

MNKIYRIIWN	SALNAWVVVS	ELTRNHTKRA	SATVKTAVLA	TLLFATVQAS	ANRAASVKDV	60
LNAGWNIKGV	KPGTTASDNV	DFVRTYDTVE	FLSADTKTTT	VNVESKDNGK	KTEVKIGAKT	120
SVIEKDKGKL	VTGKDKGENG	SSTDEGEGLV	TAKEVIDAVN	KAGWRMKTIT	ANGQTGQADK	180
FETVTSGTNV	TFASGKGTTA	TVSKDDQGNI	TVMYDVNVGD	ALNVNQLQNS	GNLDSKAVA	240
GSSGKVISGN	VSPSKGKMDT	TVNINAGNNI	EITRNGKNID	IATSMTPQFS	SVSLGAGADA	300
PTLSVDGDAL	NVGSKDNKPV	VRITNVAPGV	KEGDVTNVAQ	LKGVAQNLLN	RIDNVDGNAR	360
AGIAQAIATA	GLVQAYLPGK	SMMAIGGGTY	RGEAGYAIGY	SSISDGGNWI	IKGTASGNSR	420
GHHFGASASVG	YQW					433

SEQ ID NO:27

MNKIYRIIWN	SALNAWVVVS	ELTRNHTKRA	SATVKTAVLA	TLLFATVQAS	ANTLKAGDNL	60
KIKQFTYSLK	KDLTDLTSVG	TEKLSFSANG	NKVNITSDTK	GLNFAKETAG	TNGDTTVHLN	120
GIGSTLTDR	ASVKDVLNAG	WNIKGVKNVD	FVRTYDTVEF	LSADTKTTTV	NVESKDNGKK	180
TEVKIGAKTS	VIKEKDGLV	TGKDKGENGS	STDEGEGLVT	AKEVIDAVNK	AGWRMKTITA	240
NGQTGQADKF	ETVTSGTNVT	FASGKGTTAT	VSKDDQGNIT	VMYDVNVGDA	LNVNQLQNSG	300
WNLDSKAVAG	SSGKVISGNV	SPSKGKMDT	VNINAGNNIE	ITRNGKNIDI	ATSMTPQFSS	360
VSLGAGADAP	TLSDVDGDLN	VGSKKDNKPV	RITNVAPGVK	EGDVTNVAQL	KGVAQNLLNR	420
IDNVDGNARA	GIAQAIATAG	LVQAYLPGKS	MMAIGGGTYR	GEAGYAIGYS	SISDGGNWII	480
KGTASGNSRG	HFGASASVGY	QW				

SEQ ID NO:35

NNETDLTSVG	TEKLSFSANG	NKVNITSDTK	GLNFAKETAG	TNGDTTVHLN	GIGSTLTDTL	60
LNTGATTNVT	NDNVTDEKK	RAASVKDVLN	AGWNIKGVKP	GTTASDNVDF	VRTYDTVEFL	120
SADTKTTTTV	VESKDNGKKT	EVKIGAKTSV	IKEKDGLVT	GKDKGENGSS	TDEGEGLVTA	180
KEVIDAVNKA	GWRMKTITAN	GQTGQADKFE	TVTSGTNVTF	ASGKGTTATV	SKDDQGNITV	240
MYDVNVGDAL	NVNQLQNSGW	NLDSKAVAGS	SGKVISGNVS	PSKKGMDTV	NINAGNNIEI	300
TRNGKNIDIA	TSMTPOFSSV	SLGAGADAPT	LSVDGDALNV	GSKKDNKPVR	ITNVAPGVKE	360
GDVTNVAQLK	GVAQNLLNRI	DNVDGNARAG	IAQAIATAGL	VQAYLPGKSM	MAIGGGTYRG	420
EAGYAIGYSS	ISDGGNWIIK	GTASGNSRGH	FGASASVGYQ	W		

SEQ ID NO:36

TDETGLINVE	TEKLSFGANG	KKVNIISDTK	GLNFAKETAG	TNGDTTVHLN	GIGSTLTDML	60
LNTGATTNVT	NDNVTDEKK	RAASVKDVLN	AGWNIKGVKP	GTTASDNVDF	VRTYDTVEFL	120
SADTKTTTTV	VESKDNGKKT	EVKIGAKTSV	IKEKDGLVT	GKDKGENGSS	TDEGEGLVTA	180
KEVIDAVNKA	GWRMKTITAN	GQTGQADKFE	TVTSGTKVTF	ASGNGTTATV	SKDDQGNITV	240
KYDVNVGDAL	NVNQLQNSGW	NLDSKAVAGS	SGKVISGNVS	PSKKGMDTV	NINAGNNIEI	300
TRNGKNIDIA	TSMTPOFSSV	SLGAGADAPT	LSVDDEGALN	VGSKDANKPV	RITNVAPGVK	360
EGDVTNVAQL	KGVAQNLLNRI	IDNVNGNARA	GIAQAIATAG	LVQAYLPGKS	MMAIGGGTYL	420
GEAGYAIGYS	SISAGGNWII	KGTASGNSRG	HFGASASVGY	QW		462

SEQ ID NO:37

NNVDFVRTYD	TVEFLSADTK	TTTVNVESKD	NGKKTEVKIG	AKTSVIKEKD	GKLVTGKDKG	60
ENGSSSTDEGE	GLVTAKEVID	AVNKAGWRMK	TTTANGQTGQ	ADKFETVTSG	TNVTFASGKG	120
TTATVSKDDQ	GNITVMYDVN	VGDALNVNQL	QNSGWNLSK	AVAGSSGKVI	SGNVSPSKGK	180
MDETVNINAG	NNIEITRNGK	NIDIATSMTP	QFSSVSLGAG	ADAPTLSDVG	DALNVGSKKD	240
NKPVRITNVA	PGVKEGDVTN	VAQLKGVAQN	LNNRIDNVDG	NARAGIAQAI	ATAGLVQAYL	300
PGKSMMAIGG	GTYRGEAGYA	IGYSSISDGG	NWIIKGTASG	NSRGHFGASA	SVGYQW	356

SEQ ID NO:38

NRAASVKDVL	NAGWNIKGVK	PGTTASDNVD	FVRTYDTVEF	LSADTKTTTTV	NVESKDNGKK	60
TEVKIGAKTS	VIKEKDGLV	TGKDKGENGS	STDEGEGLVT	AKEVIDAVNK	AGWRMKTITTA	120
NGQTGQADKF	ETVTSGTNVT	FASGKGTTAT	VSKDDQGNIT	VMYDVNVGDA	LVNVLQNSG	180
WNLSKAVAG	SSGKVISGNV	SPSKGMDTV	VNINAGNNIE	ITRNGKNIDI	ATSMTPQFSS	240
VSLGAGADAP	TLSDVDGALN	VGSKKDNKPV	RITNVAPGVK	EGDVTNVAQL	KGVAQNLLNRI	300
IDNVGNARA	GIAQAIATAG	LVQAYLPGKS	MMAIGGGTYR	GEAGYAIGYS	SISDGGNWII	360
KGTASGNSRG	HFGASASVGY	QW				

SEQ ID NO:39

S	ANTLKAGDNLKIKQFTYSLK	KDLTDLTSVG	TEKLSFSANG	NKVNITSDTK	GLNFAKETAG	
TNGDTTVHLN	GIGSTLTDRA	ASVKDVLNAG	WNIKGVKND	FVRTYDTVEF	LSADTKTTTTV	
NVESKDNGKK	TEVKIGAKTS	VIKEKDGLV	TGKDKGENGS	STDEGEGLVT	AKEVIDAVNK	
AGWRMKTITTA	NGQTGQADKF	ETVTSGTNVT	FASGKGTTAT	VSKDDQGNIT	VMYDVNVGDA	
LVNVLQNSG	WNLSKAVAG	SSGKVISGNV	SPSKGMDTV	VNINAGNNIE	ITRNGKNIDI	
ATSMTPQFSS	VSLGAGADAP	TLSDVDGALN	VGSKKDNKPV	RITNVAPGVK	EGDVTNVAQL	
KGVAQNLLNRI	IDNVGNARA	GIAQAIATAG	LVQAYLPGKS	MMAIGGGTYR	GEAGYAIGYS	
SISDGGNWII	KGTASGNSRG	HFGASASVGY	QW			

ClustalW (v1.4) multiple sequence alignment

2 Sequences Aligned Alignment Score = 2831
Gaps Inserted = 1 Conserved Identities = 489

Pairwise Alignment Mode: Slow

Pairwise Alignment Parameters:

Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1

Similarity Matrix: id

Multiple Alignment Parameters:

Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1

Delay Divergent = 40% Gap Distance = 8

Similarity Matrix: id

Processing time: 0.4 seconds

1. SEQ ID NO 23 vs. SEQ ID NO 24

Aligned Length = 513 Gaps = 1
Identities = 489 (95%) Similarities = 1 (0%)

```
SEQ ID NO 23   1 MNKIYRIIWNALNAWVVVSELTRNHTKRASATVKTAVLATLLFATVQAS  50
SEQ ID NO 24   1 MNKIYRIIWNALNAWVAVSELTRNHTKRASATVKTAVLATLLFATVQAN  50
                *****

SEQ ID NO 23   51 ANNETDLTSVGTEKLSFSANGNKVNITSDTKGLNFAKETAGTNGDTTVHL  100
SEQ ID NO 24   51 ATDETGLINVETEKLSFGANGKKVNIISDTKGLNFAKETAGTNGDTTVHL  100
                *  *  *  *  *****

SEQ ID NO 23   101 NGIGSTLTDTLLNTGATTNVTNDNVTDDKRAASVKDVLNAGWNIKGVK  150
SEQ ID NO 24   101 NGIGSTLTDMLLNTGATTNVTNDNVTDDKRAASVKDVLNAGWNIKGVK  150
                *****

SEQ ID NO 23   151 PGTTASDNVDFVRTYDTVEFLSADTKTTTVNVESKDNGKKTEVKIGAKTS  200
SEQ ID NO 24   151 PGTTASDNVDFVRTYDTVEFLSADTKTTTVNVESKDNGKKTEVKIGAKTS  200
                *****

SEQ ID NO 23   201 VIKEKDGLVTGKDKGENSSSTDEGEGLVTAKEVIDAVNKAGWRMKTTTA  250
SEQ ID NO 24   201 VIKEKDGLVTGKDKGENSSSTDEGEGLVTAKEVIDAVNKAGWRMKTTTA  250
                *****

SEQ ID NO 23   251 NGQTGQADKFETVTSNTVFASGKGTATVSKDDQGNITVMYDVNVGDA  300
SEQ ID NO 24   251 NGQTGQADKFETVTSNTVFASGNGTTATVSKDDQGNITVKYDVNVGDA  300
                *****

SEQ ID NO 23   301 LNVNQLQNSGWNLDKAVAGSSGKVISGNVSPSKGKMDETVNINAGNNIE  350
SEQ ID NO 24   301 LNVNQLQNSGWNLDKAVAGSSGKVISGNVSPSKGKMDETVNINAGNNIE  350
                *****

SEQ ID NO 23   351 ITRNGKNIDIATSMTPQFSSVSLGAGADAPTLSDVG-DALNVGSKKDNKP  399
SEQ ID NO 24   351 ITRNGKNIDIATSMTPQFSSVSLGAGADAPTLSDVDEGALNVGSKDANKP  400
                *****

SEQ ID NO 23   400 VRITNVAPGVKEGDVTNVAQLKGVAQNLNNRIDNVNAGNARAGIAQAIATA  449
SEQ ID NO 24   401 VRITNVAPGVKEGDVTNVAQLKGVAQNLNNRIDNVNAGNARAGIAQAIATA  450
                *****

SEQ ID NO 23   450 GLVQAYLPKGSMAIGGGTYRGEAGYAIGYSSISDGGNWIIGKTASGNSR  499
SEQ ID NO 24   451 GLVQAYLPKGSMAIGGGTYLGEAGYAIGYSSISAGGNWIIGKTASGNSR  500
                *****
```

of 2

SEQ ID NO 23 500 GHFGASASVGYQW 512
SEQ ID NO 24 501 GHFGASASVGYQW 513

of 2

ClustalW (v1.4) multiple sequence alignment

2 Sequences Aligned Alignment Score = 2374
Gaps Inserted = 1 Conserved Identities = 407

Pairwise Alignment Mode: Slow

Pairwise Alignment Parameters:

Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1
Similarity Matrix: id

Multiple Alignment Parameters:

Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1
Delay Divergent = 40% Gap Distance = 8
Similarity Matrix: id

Processing time: 0.3 seconds

1. SEQ ID NO 23 vs. SEQ ID NO 25

Aligned Length = 512 Gaps = 1
Identities = 407 (79%) Similarities = 0 (0%)

```
SEQ ID NO 23   1 MNKIYRIIWNALNAWVVVSELTRNHTKRASATVKTAVLATLLFATVQAS  50
SEQ ID NO 25   1 MNKIYRIIWNALNAWVVVSELTRNHTKRASATVKTAVLATLLFATVQAS  50
                *****

SEQ ID NO 23   51 ANNETDLTSVGTEKLSFSANGNKVNITSDTKGLNFAKETAGTNGDTTVHL 100
SEQ ID NO 25   51 AN----- 52
                **

SEQ ID NO 23  101 NGIGSTLTDLLNTGATTNVTNDNVTDEKKRAASVKDVLNAGWNIKGVK 150
SEQ ID NO 25   53 ----- 52

SEQ ID NO 23  151 PGTTASDNVDFVRTYDVEFLSADTKTTTVNVESKDNGKKTEVKIGAKTS 200
SEQ ID NO 25   53 -----NVDFVRTYDVEFLSADTKTTTVNVESKDNGKKTEVKIGAKTS  95
                *****

SEQ ID NO 23  201 VIKEKDGKLVTKGDKGENGSSTDEGEGLVTAKEVIDAVNKAGWRMKTTTA 250
SEQ ID NO 25   96 VIKEKDGKLVTKGDKGENGSSTDEGEGLVTAKEVIDAVNKAGWRMKTTTA 145
                *****

SEQ ID NO 23  251 NGQTGQADKFETVTSGTNVTFASGKGTATVSKDDQGNITVMYDVNVGDA 300
SEQ ID NO 25  146 NGQTGQADKFETVTSGTNVTFASGKGTATVSKDDQGNITVMYDVNVGDA 195
                *****

SEQ ID NO 23  301 LNVNQLQNSGWNLDSKAVAGSSGKVISGNVSPSKGKMDETVNINAGNNIE 350
SEQ ID NO 25  196 LNVNQLQNSGWNLDSKAVAGSSGKVISGNVSPSKGKMDETVNINAGNNIE 245
                *****

SEQ ID NO 23  351 ITRNGKNIDIATSMTPQFSSVSLGAGADAPTLSVDGDALNVGSKKDNKPV 400
SEQ ID NO 25  246 ITRNGKNIDIATSMTPQFSSVSLGAGADAPTLSVDGDALNVGSKKDNKPV 295
                *****

SEQ ID NO 23  401 RITNVAPGVKEGDVTNVAQLKGVAQNLNNRIDNVDGNARAGIAQAIATAG 450
SEQ ID NO 25  296 RITNVAPGVKEGDVTNVAQLKGVAQNLNNRIDNVDGNARAGIAQAIATAG 345
                *****

SEQ ID NO 23  451 LVQAYLPGKSMMIAIGGGTYRGEAGYAIGYSSISDGGNWIIGKTASGNSRG 500
SEQ ID NO 25  346 LVQAYLPGKSMMIAIGGGTYRGEAGYAIGYSSISDGGNWIIGKTASGNSRG 395
                *****
```

92

SEQ ID NO 23 501 HFGASASVG YQW 512
SEQ ID NO 25 396 HFGASASVG YQW 407

of 2

ClustalW (v1.4) multiple sequence alignment

2 Sequences Aligned Alignment Score = 2530
Gaps Inserted = 1 Conserved Identities = 433

Pairwise Alignment Mode: Slow

Pairwise Alignment Parameters:

Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1

Similarity Matrix: id

Multiple Alignment Parameters:

Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1

Delay Divergent = 40% Gap Distance = 8

Similarity Matrix: id

Processing time: 0.3 seconds

1. SEQ ID NO 23 vs. SEQ ID NO 26

Aligned Length = 512 Gaps = 1
Identities = 433 (84%) Similarities = 0 (0%)

```
SEQ ID NO 23   1 MNKIYRIIWNALNAWVVVSELTRNHTKRASATVKTAVLATLLFATVQAS  50
SEQ ID NO 26   1 MNKIYRIIWNALNAWVVVSELTRNHTKRASATVKTAVLATLLFATVQAS  50
*****

SEQ ID NO 23   51 ANNETDLTSVGTEKLSFSANGNKVNITSDTKGLNFAKETAGTNGDTTVHL 100
SEQ ID NO 26   51 AN----- 52
**

SEQ ID NO 23  101 NGIGSTLTDLLNTGATTNVTNDNVTDEKKRAASVKDVLNAGWNIKGVK 150
SEQ ID NO 26   53 -----RAASVKDVLNAGWNIKGVK 71
*****

SEQ ID NO 23  151 PGTTASDNVDFVRTYDTVEFLSADTKTTTVNVESKDNGKKTEVKIGAKTS 200
SEQ ID NO 26   72 PGTTASDNVDFVRTYDTVEFLSADTKTTTVNVESKDNGKKTEVKIGAKTS 121
*****

SEQ ID NO 23  201 VIKEKDGLVTGKDKGENGSSTDEGEGLVTAKEVIDAVNKAGWRMKTTTA 250
SEQ ID NO 26  122 VIKEKDGLVTGKDKGENGSSTDEGEGLVTAKEVIDAVNKAGWRMKTTTA 171
*****

SEQ ID NO 23  251 NGQTGQADKFETVTSGTNVTFASGKGTATVSKDDQGNITVMYDVNVGDA 300
SEQ ID NO 26  172 NGQTGQADKFETVTSGTNVTFASGKGTATVSKDDQGNITVMYDVNVGDA 221
*****

SEQ ID NO 23  301 LNVNQLQNSGWNLDKAVAGSSGKVISGNVSPSKGKMDETVNINAGNNIE 350
SEQ ID NO 26  222 LNVNQLQNSGWNLDKAVAGSSGKVISGNVSPSKGKMDETVNINAGNNIE 271
*****

SEQ ID NO 23  351 ITRNGKNIDIATSMTPQFSSVSLGAGADAPTLSDGDALNVGSKKDNKPV 400
SEQ ID NO 26  272 ITRNGKNIDIATSMTPQFSSVSLGAGADAPTLSDGDALNVGSKKDNKPV 321
*****

SEQ ID NO 23  401 RITNVAPGVKEGDVTNVAQLKGVAQNLNNRIDNVDGNARAGIAQAIATAG 450
SEQ ID NO 26  322 RITNVAPGVKEGDVTNVAQLKGVAQNLNNRIDNVDGNARAGIAQAIATAG 371
*****

SEQ ID NO 23  451 LVQAYLPGKSMMAIGGGTYRGEAGYAIGYSSISDGGNWIKGTASGNSRG 500
SEQ ID NO 26  372 LVQAYLPGKSMMAIGGGTYRGEAGYAIGYSSISDGGNWIKGTASGNSRG 421
*****
```

q²

SEQ ID NO 23 501 HFGASASVG YQW 512
SEQ ID NO 26 422 HFGASASVG YQW 433

of 2

ClustalW (v1.4) multiple sequence alignment

2 Sequences Aligned Alignment Score = 2819
Gaps Inserted = 3 Conserved Identities = 481

Pairwise Alignment Mode: Slow
Pairwise Alignment Parameters:
 Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1
 Similarity Matrix: id

Multiple Alignment Parameters:
 Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1
 Delay Divergent = 40% Gap Distance = 8
 Similarity Matrix: id

Processing time: 0.4 seconds

1. SEQ ID NO 23 vs. SEQ ID NO 27

Aligned Length = 531 Gaps = 3
Identities = 481 (93%) Similarities = 0 (0%)

```
SEQ ID NO 23   1 MNKIYRIIWNALNAWVVVSELTRNHTKRASATVKTAVLATLLFATVQAS  50
SEQ ID NO 27   1 MNKIYRIIWNALNAWVVVSELTRNHTKRASATVKTAVLATLLFATVQAS  50
*****

SEQ ID NO 23   51 AN-----NETDLTSVGTEKLSFSANGNKVNITSDTK  81
SEQ ID NO 27   51 ANTLKAGDNLKIKQFTYSLKKDLTDLTSVGTEKLSFSANGNKVNITSDTK 100
**                               *****

SEQ ID NO 23   82 GLNFAKETAGTNGDTTVHLNGIGSTLTDLLNTGATTNVTNDNVTDDEKK 131
SEQ ID NO 27  101 GLNFAKETAGTNGDTTVHLNGIGSTLTD----- 128
*****

SEQ ID NO 23  132 RAASVKDVLNAGWNIKGVPKGTASDNVDFVRTYDTVEFLSADTKTTTVN 181
SEQ ID NO 27  129 RAASVKDVLNAGWNIKGVK-----NVDFVRTYDTVEFLSADTKTTTVN 171
*****

SEQ ID NO 23  182 VESKDNGKKTEVKIGAKTSVIKEKDGLVTGKDKGENGSSTDEGEGLVTA 231
SEQ ID NO 27  172 VESKDNGKKTEVKIGAKTSVIKEKDGLVTGKDKGENGSSTDEGEGLVTA 221
*****

SEQ ID NO 23  232 KEVIDAVNKAGWRMKTITTANGQTGQADKFETVTSGTNVTTFASGKGTTATV 281
SEQ ID NO 27  222 KEVIDAVNKAGWRMKTITTANGQTGQADKFETVTSGTNVTTFASGKGTTATV 271
*****

SEQ ID NO 23  282 SKDDQGNITVMYDVNVGDALNVNQLQNSGWNLDSKAVAGSSGKVISGNVS 331
SEQ ID NO 27  272 SKDDQGNITVMYDVNVGDALNVNQLQNSGWNLDSKAVAGSSGKVISGNVS 321
*****

SEQ ID NO 23  332 PSKGKMDETVNIAGNNIEITRNGKNIDIATSMTPQFSSVSLGAGADAPT 381
SEQ ID NO 27  322 PSKGKMDETVNIAGNNIEITRNGKNIDIATSMTPQFSSVSLGAGADAPT 371
*****

SEQ ID NO 23  382 LSVDGDALNVGSKKDNKPVKITNVPAGVKEGDVTNVAQLKGVAQNLNNRI 431
SEQ ID NO 27  372 LSVDGDALNVGSKKDNKPVKITNVPAGVKEGDVTNVAQLKGVAQNLNNRI 421
*****

SEQ ID NO 23  432 DNVDGNARAGIAQAIATAGLVQAYLPGKSMMIAIGGGTYRGEAGYAIGYSS 481
SEQ ID NO 27  422 DNVDGNARAGIAQAIATAGLVQAYLPGKSMMIAIGGGTYRGEAGYAIGYSS 471
*****
```


23 VS 27

Friday, 25 August 2006 11:22 AM

Page 2

of 2

SEQ ID NO 23 482 ISDGGNWIIGKTASGNSRGHFGASASVGYQW 512
SEQ ID NO 27 472 ISDGGNWIIGKTASGNSRGHFGASASVGYQW 502

df2

ClustalW (v1.4) multiple sequence alignment

2 Sequences Aligned Alignment Score = 2681
Gaps Inserted = 0 Conserved Identities = 461

Pairwise Alignment Mode: Slow
Pairwise Alignment Parameters:
 Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1
 Similarity Matrix: id

Multiple Alignment Parameters:
 Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1
 Delay Divergent = 40% Gap Distance = 8
 Similarity Matrix: id

Processing time: 0.4 seconds

1. SEQ ID NO 23 vs. SEQ ID NO 35

Aligned Length = 512 Gaps = 0
Identities = 461 (90%) Similarities = 0 (0%)

```
SEQ ID NO 23   1 MNKIYRIIWNLSALNAWVVVSELTRNHTKRASATVKTAVLATLLFATVQAS  50
SEQ ID NO 35   1                                     0

SEQ ID NO 23   51 ANNETDLTSVGTEKLSFSANGNKVNITSDTKGLNFAKETAGTNGDTTVHL  100
SEQ ID NO 35   1  NNETDLTSVGTEKLSFSANGNKVNITSDTKGLNFAKETAGTNGDTTVHL  49
*****

SEQ ID NO 23  101 NGIGSTLTDTLNLTGATTNVTNDNVTDDDEKKRAASVKDVLNAGWNIKGVK  150
SEQ ID NO 35   50 NGIGSTLTDTLNLTGATTNVTNDNVTDDDEKKRAASVKDVLNAGWNIKGVK  99
*****

SEQ ID NO 23  151 PGTTASDNVDFVRTYDTVEFLSADTKTTTVNVESKDNGKKTEVKIGAKTS  200
SEQ ID NO 35  100 PGTTASDNVDFVRTYDTVEFLSADTKTTTVNVESKDNGKKTEVKIGAKTS  149
*****

SEQ ID NO 23  201 VIKEDGKLVTKGDKGENGSSTDEGEGLVTAKEVIDAVNKAGWRMKTTTA  250
SEQ ID NO 35  150 VIKEDGKLVTKGDKGENGSSTDEGEGLVTAKEVIDAVNKAGWRMKTTTA  199
*****

SEQ ID NO 23  251 NGQTGQADKFETVTSGTNVTFASGKGTATVSKDDQGNITVMYDVNVGDA  300
SEQ ID NO 35  200 NGQTGQADKFETVTSGTNVTFASGKGTATVSKDDQGNITVMYDVNVGDA  249
*****

SEQ ID NO 23  301 LNVNQLQNSGWNLDSKAVAGSSGKVISGNVSPSKGKMDETVNINAGNNIE  350
SEQ ID NO 35  250 LNVNQLQNSGWNLDSKAVAGSSGKVISGNVSPSKGKMDETVNINAGNNIE  299
*****

SEQ ID NO 23  351 ITRNGKNIDIATSMTPQFSSVSLGAGADAPTLSDVDGALNVGSKKDNKPV  400
SEQ ID NO 35  300 ITRNGKNIDIATSMTPQFSSVSLGAGADAPTLSDVDGALNVGSKKDNKPV  349
*****

SEQ ID NO 23  401 RITNVAPGVKEGDVTNVAQLKGVAQNLNRRIDNVDGNARAGIAQAIATAG  450
SEQ ID NO 35  350 RITNVAPGVKEGDVTNVAQLKGVAQNLNRRIDNVDGNARAGIAQAIATAG  399
*****

SEQ ID NO 23  451 LVQAYLPGKSMMAIGGGTYRGEAGYAIGYSSISDGGNWIKGTASGNSRG  500
SEQ ID NO 35  400 LVQAYLPGKSMMAIGGGTYRGEAGYAIGYSSISDGGNWIKGTASGNSRG  449
*****
```

of 2

SEQ ID NO 23 501 HFGASASVGYQW 512
SEQ ID NO 35 450 HFGASASVGYQW 461

```

SEQ ID NO 23 450 GLVQAYLPGKSMAIGGGTYRGEAGYAIGYSSISDGGNWIKGTASGNSR 499
SEQ ID NO 36 400 GLVQAYLPGKSMAIGGGTYLGEAGYAIGYSSISAGGNWIKGTASGNSR 449
*****

```

of 2

SEQ ID NO 23 500 GHFGASASVGYQW 512
SEQ ID NO 36 450 GHFGASASVGYQW 462

of 2

2 Sequences Aligned Alignment Score = 2075
Gaps Inserted = 0 Conserved Identities = 355

Multiple Alignment Parameters:
 Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1
 Delay Divergent = 40% Gap Distance = 8
 Similarity Matrix: id

1. SEQ ID NO 23 vs. SEQ ID NO 37

SEQ ID NO 23 451 LVQAYLPKGSMMMAIGGGTYRGEAGYAIGYSSISDGGNWIICKGTASGNSRG 500
SEQ ID NO 37 295 LVQAYLPKGSMMMAIGGGTYRGEAGYAIGYSSISDGGNWIICKGTASGNSRG 344

of 2

SEQ ID NO 23 501 HFGASASVG YQW 512
SEQ ID NO 37 345 HFGASASVG YQW 356

of 2

ClustalW (v1.4) multiple sequence alignment

2 Sequences Aligned Alignment Score = 2229
Gaps Inserted = 0 Conserved Identities = 381

Pairwise Alignment Mode: Slow

Pairwise Alignment Parameters:

Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1
Similarity Matrix: id

Multiple Alignment Parameters:

Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1
Delay Divergent = 40% Gap Distance = 8
Similarity Matrix: id

Processing time: 0.3 seconds

1. SEQ ID NO 23 vs. SEQ ID NO 38

Aligned Length = 512 Gaps = 0
Identities = 381 (74%) Similarities = 0 (0%)

```
SEQ ID NO 23   1 MNKIYRIIWSALNAWVVVSELTRNHTKRASATVKTAVLATLLFATVQAS  50
SEQ ID NO 38   1                                     0

SEQ ID NO 23  51 ANNETDLTSVGTEKLSFSANGNKVNITSDTKGLNFAKETAGTNGDTTVHL 100
SEQ ID NO 38   1                                     0

SEQ ID NO 23 101 NGIGSTLTDLLNTGATTNVTNDNVTDDEKKRAASVKDVLNAGWNIKGVK 150
SEQ ID NO 38   1                               NRAASVKDVLNAGWNIKGVK 20
                *****

SEQ ID NO 23 151 PGTTASDNVDFVRTYDTVEFLSADTKTTTVNVESKDNGKKTEVKIGAKTS 200
SEQ ID NO 38  21 PGTTASDNVDFVRTYDTVEFLSADTKTTTVNVESKDNGKKTEVKIGAKTS  70
                *****

SEQ ID NO 23 201 VIKEKDGKLVTKGDKGENGSSTDEGEGLVTAKEVIDAVNKAGWRMKTITTA 250
SEQ ID NO 38  71 VIKEKDGKLVTKGDKGENGSSTDEGEGLVTAKEVIDAVNKAGWRMKTITTA 120
                *****

SEQ ID NO 23 251 NGQTGQADKFETVTSGTNVTFASGKGTATVSKDDQGNITVMYDVNVGDA 300
SEQ ID NO 38 121 NGQTGQADKFETVTSGTNVTFASGKGTATVSKDDQGNITVMYDVNVGDA 170
                *****

SEQ ID NO 23 301 LNVNQLQNSGWNLDSKAVAGSSGKVISGNVSPSKGKMDETVNINAGNNIE 350
SEQ ID NO 38 171 LNVNQLQNSGWNLDSKAVAGSSGKVISGNVSPSKGKMDETVNINAGNNIE 220
                *****

SEQ ID NO 23 351 ITRNGKNIDIATSMTPQFSSVSLGAGADAPTLSDVDGALNVGSKKDNKPV 400
SEQ ID NO 38 221 ITRNGKNIDIATSMTPQFSSVSLGAGADAPTLSDVDGALNVGSKKDNKPV 270
                *****

SEQ ID NO 23 401 RITNVAPGVKEGDVTNVAQLKGVAQNLNRRIDNVDGNARAGIAQAIATAG 450
SEQ ID NO 38 271 RITNVAPGVKEGDVTNVAQLKGVAQNLNRRIDNVDGNARAGIAQAIATAG 320
                *****

SEQ ID NO 23 451 LVQAYLPGKSMMAIGGGTYRGEAGYAIGYSSISDGGNWIKGTASGNSRG 500
SEQ ID NO 38 321 LVQAYLPGKSMMAIGGGTYRGEAGYAIGYSSISDGGNWIKGTASGNSRG 370
                *****
```


df2

SEQ ID NO 23 501 HFGASASVG YQW 512
SEQ ID NO 38 371 HFGASASVG YQW 382

of 2

ClustalW (v1.4) multiple sequence alignment

2 Sequences Aligned Alignment Score = 2510
Gaps Inserted = 2 Conserved Identities = 432

Pairwise Alignment Mode: Slow

Pairwise Alignment Parameters:

Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1
Similarity Matrix: id

Multiple Alignment Parameters:

Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1
Delay Divergent = 40% Gap Distance = 8
Similarity Matrix: id

Processing time: 0.3 seconds

1. SEQ ID NO 23 vs. SEQ ID NO 39

Aligned Length = 512 Gaps = 2
Identities = 432 (84%) Similarities = 3 (0%)

```
SEQ ID NO 23   1 MNKIYRIIWSALNAWVVVSELTRNHTKRASATVKTAVLATLLFATVQAS  50
SEQ ID NO 39   1                                     SANTLKAGDNLKIKQFTYSL  20
                                     **      *

SEQ ID NO 23   51 ANNETDLTSVGTEKLSFSANGNKVNITSDTKGLNFAKETAGTNGDTTVHL 100
SEQ ID NO 39   21 KKDLTDLTSVGTEKLSFSANGNKVNITSDTKGLNFAKETAGTNGDTTVHL  70
               *****

SEQ ID NO 23   101 NGIGSTLTDLTLLNTGATTNVTNDNVTDDKRAASVKDVLNAGWNIKGVK 150
SEQ ID NO 39   71 NGIGSTLTD-----RAASVKDVLNAGWNIKGVK  98
               *****

SEQ ID NO 23   151 PGTTASDNVDFVRTYDTVEFLSADTKTTTVNVESKDNGKKTEVKIGAKTS 200
SEQ ID NO 39   99 -----NVDFVRTYDTVEFLSADTKTTTVNVESKDNGKKTEVKIGAKTS 141
               *****

SEQ ID NO 23   201 VIKEDGKLVGTGKDKGENGSSTDEGEGLVTAKEVIDAVNKAGWRMKTTTA 250
SEQ ID NO 39   142 VIKEDGKLVGTGKDKGENGSSTDEGEGLVTAKEVIDAVNKAGWRMKTTTA 191
               *****

SEQ ID NO 23   251 NGQTGQADKFETVTSGTNVTFASGKGTATVSKDDQGNITVMYDVNVGDA 300
SEQ ID NO 39   192 NGQTGQADKFETVTSGTNVTFASGKGTATVSKDDQGNITVMYDVNVGDA 241
               *****

SEQ ID NO 23   301 LNVNQLQNSGWNLDSKAVAGSSGKVISGNVSPSKGKMDETVNINAGNNIE 350
SEQ ID NO 39   242 LNVNQLQNSGWNLDSKAVAGSSGKVISGNVSPSKGKMDETVNINAGNNIE 291
               *****

SEQ ID NO 23   351 ITRNGKNIDIATSMTPQFSSVSLGAGADAPTLSDVDGALNVGSKKDNKPV 400
SEQ ID NO 39   292 ITRNGKNIDIATSMTPQFSSVSLGAGADAPTLSDVDGALNVGSKKDNKPV 341
               *****

SEQ ID NO 23   401 RITNVAPGVKEGDVTNVAQLKGVAQNLNNRIDNVDGNARAGIAQAIATAG 450
SEQ ID NO 39   342 RITNVAPGVKEGDVTNVAQLKGVAQNLNNRIDNVDGNARAGIAQAIATAG 391
               *****

SEQ ID NO 23   451 LVQAYLPGKSMMIAIGGGTYRGEAGYAIGYSSISDGGNWIKGTASGNSRG 500
SEQ ID NO 39   392 LVQAYLPGKSMMIAIGGGTYRGEAGYAIGYSSISDGGNWIKGTASGNSRG 441
               *****
```

2

SEQ ID NO 23 501 HFGASASVG YQW 512
SEQ ID NO 39 442 HFGASASVG YQW 453

of 2

ClustalW (v1.4) multiple sequence alignment

2 Sequences Aligned Alignment Score = 2681
Gaps Inserted = 0 Conserved Identities = 461

Pairwise Alignment Mode: Slow

Pairwise Alignment Parameters:

Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1

Similarity Matrix: id

Multiple Alignment Parameters:

Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1

Delay Divergent = 40% Gap Distance = 8

Similarity Matrix: id

Processing time: 0.4 seconds

1. SEQ ID NO 35 vs. SEQ ID NO 23

Aligned Length = 512 Gaps = 0
Identities = 461 (90%) Similarities = 0 (0%)

```
SEQ ID NO 35      1
SEQ ID NO 23      1 MNKIYRIIWSALNAWVVSELTRNHTKRASATVKTAVLATLLFATVQAS 50

SEQ ID NO 35      1 NNETDLTSVGTEKLSFSANGNKVNITSDTKGLNFAKETAGTNGDTTVHL 49
SEQ ID NO 23      51 ANNETDLTSVGTEKLSFSANGNKVNITSDTKGLNFAKETAGTNGDTTVHL 100
*****

SEQ ID NO 35      50 NGIGSTLTDTLLNTGATTNVTNDNVTDEKKRAASVKDVLNAGWNIKGVK 99
SEQ ID NO 23      101 NGIGSTLTDTLLNTGATTNVTNDNVTDEKKRAASVKDVLNAGWNIKGVK 150
*****

SEQ ID NO 35      100 PGTTASDNVDFVRTYDTVEFLSADTKTTTVNVESKDNGKKTEVKIGAKTS 149
SEQ ID NO 23      151 PGTTASDNVDFVRTYDTVEFLSADTKTTTVNVESKDNGKKTEVKIGAKTS 200
*****

SEQ ID NO 35      150 VIKEKDGLVTGKDKGENSSSTDEGEGLVTAKEVIDAVNKAGWRMKTSTA 199
SEQ ID NO 23      201 VIKEKDGLVTGKDKGENSSSTDEGEGLVTAKEVIDAVNKAGWRMKTSTA 250
*****

SEQ ID NO 35      200 NGQTGQADKFETVTSGTNVTFASGKGTATVSKDDQGNITVMYDVNVGDA 249
SEQ ID NO 23      251 NGQTGQADKFETVTSGTNVTFASGKGTATVSKDDQGNITVMYDVNVGDA 300
*****

SEQ ID NO 35      250 LNVNQLQNSGWNLDKAVAGSSGKVISGNVSPSKGKMDETVNINAGNNIE 299
SEQ ID NO 23      301 LNVNQLQNSGWNLDKAVAGSSGKVISGNVSPSKGKMDETVNINAGNNIE 350
*****

SEQ ID NO 35      300 ITRNGKNIDIATSMTPQFSSVSLGAGADAPTLSDGDALNVGSKKDNKPV 349
SEQ ID NO 23      351 ITRNGKNIDIATSMTPQFSSVSLGAGADAPTLSDGDALNVGSKKDNKPV 400
*****

SEQ ID NO 35      350 RITNVAPGVKEGDVTNVAQLKGVAQNLNNRIDNVDGNARAGIAQAIATAG 399
SEQ ID NO 23      401 RITNVAPGVKEGDVTNVAQLKGVAQNLNNRIDNVDGNARAGIAQAIATAG 450
*****

SEQ ID NO 35      400 LVQAYLPKGSMMIAIGGGTYRGEAGYAIGYSSISDGGNWIIGKTASGNSRG 449
SEQ ID NO 23      451 LVQAYLPKGSMMIAIGGGTYRGEAGYAIGYSSISDGGNWIIGKTASGNSRG 500
*****
```

of 2

SEQ ID NO 35 450 HFGASASVGYQW 461
SEQ ID NO 23 501 HFGASASVGYQW 512

ClustalW (v1.4) multiple sequence alignment

2 Sequences Aligned Alignment Score = 2554
Gaps Inserted = 1 Conserved Identities = 440

Pairwise Alignment Mode: Slow

Pairwise Alignment Parameters:

Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1

Similarity Matrix: id

Multiple Alignment Parameters:

Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1

Delay Divergent = 40% Gap Distance = 8

Similarity Matrix: id

Processing time: 0.3 seconds

1. SEQ ID NO 35 vs. SEQ ID NO 24

Aligned Length = 513 Gaps = 1
Identities = 440 (85%) Similarities = 1 (0%)

```
SEQ ID NO 35      1                                     0
SEQ ID NO 24      1 MNKIYRIIWNLSALNAWVAVSELTRNHTKRASATVKTAVLATLLFATVQAN 50

SEQ ID NO 35      1 NNETDLTSVGTEKLSFSANGNKVNITSDTKGLNFAKETAGTNGDTTVHL 49
SEQ ID NO 24      51 ATDETGLINVETEKLSFGANGKKVNIISDTKGLNFAKETAGTNGDTTVHL 100
      * * * * *

SEQ ID NO 35      50 NGIGSTLTDLLNTGATTNVTNDNVTDDKKRAASVKDVLNAGWNIKGVK 99
SEQ ID NO 24      101 NGIGSTLTDMLLNTGATTNVTNDNVTDDKKRAASVKDVLNAGWNIKGVK 150
      *****

SEQ ID NO 35      100 PGTTASDNVDFVRTYDVEFLSADTKTTTVNVESKDNGKKTEVKIGAKTS 149
SEQ ID NO 24      151 PGTTASDNVDFVRTYDVEFLSADTKTTTVNVESKDNGKKTEVKIGAKTS 200
      *****

SEQ ID NO 35      150 VIKEDGKLVGTGKDKGENSSSTDEGEGLVTAKEVIDAVNKAGWRMKTITA 199
SEQ ID NO 24      201 VIKEDGKLVGTGKDKGENSSSTDEGEGLVTAKEVIDAVNKAGWRMKTITA 250
      *****

SEQ ID NO 35      200 NGQTGQADKFETVTSGTNVTFASGKGTATVSKDDQGNITVMYDVNVGDA 249
SEQ ID NO 24      251 NGQTGQADKFETVTSGTKVTFASGNGTTATVSKDDQGNITVKYDVNVGDA 300
      *****

SEQ ID NO 35      250 LNVNQLQNSGWNLDKAVAGSSGKVISGNVSPSKGKMDETVNINAGNNIE 299
SEQ ID NO 24      301 LNVNQLQNSGWNLDKAVAGSSGKVISGNVSPSKGKMDETVNINAGNNIE 350
      *****

SEQ ID NO 35      300 ITRNGKNIDIATSMTPQFSSVSLGAGADAPTLSDVG-DALNVGSKKDNKP 348
SEQ ID NO 24      351 ITRNGKNIDIATSMTPQFSSVSLGAGADAPTLSDVDEGALNVGSKDANKP 400
      *****

SEQ ID NO 35      349 VRITNVAPGVKEGDVTNVAQLKGVAQNLNNRIDNVNAGNARAGIAQAIATA 398
SEQ ID NO 24      401 VRITNVAPGVKEGDVTNVAQLKGVAQNLNNRIDNVNAGNARAGIAQAIATA 450
      *****

SEQ ID NO 35      399 GLVQAYLPGKSMMAIGGGTYRGEAGYAIGYSSISDGGNWIIGKTASGNSR 448
SEQ ID NO 24      451 GLVQAYLPGKSMMAIGGGTYLGEAGYAIGYSSISAGGNWIIGKTASGNSR 500
      *****
```

of 2

SEQ ID NO 35 449 GHFGASASVG YQW 461
SEQ ID NO 24 501 GHFGASASVG YQW 513

of 1

ClustalW (v1.4) multiple sequence alignment

2 Sequences Aligned Alignment Score = 2138
Gaps Inserted = 2 Conserved Identities = 367

Pairwise Alignment Mode: Slow
Pairwise Alignment Parameters:
 Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1
 Similarity Matrix: id

Multiple Alignment Parameters:
 Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1
 Delay Divergent = 40% Gap Distance = 8
 Similarity Matrix: id

Processing time: 0.3 seconds

1. SEQ ID NO 35 vs. SEQ ID NO 25

Aligned Length = 461 Gaps = 2
Identities = 367 (79%) Similarities = 11 (2%)

```
SEQ ID NO 35      1 NNETDLTSVGTEKLSFSANGNKVNITSDTKGLNFAKETAGTNGDTTVHLN  50
SEQ ID NO 25      1                                     MN      2
                                     *

SEQ ID NO 35     51 GIGSTLTDLLNTGATTNVTNDNVTDDEKKRAASVKDVLNAGWNIKGVPK 100
SEQ ID NO 25      3 KIYRIIWNLSALNAWVVSELTRNHT---KRASATVKTAVLATLLFATVQA  49
      *      .  **      .  *  *      *  .  *  *  *      *      *

SEQ ID NO 35    101 GTTASDNVDFVRTYDVEFLSADTKTTTVNVESKDNGKKTEVKIGAKTSV 150
SEQ ID NO 25     50 S---ANNVDFVRTYDVEFLSADTKTTTVNVESKDNGKKTEVKIGAKTSV  96
      *****

SEQ ID NO 35    151 IKEKDGKLVTKGDKGENGSSTDEGEGLVTAKEVIDAVNKAGWRMKTITAN 200
SEQ ID NO 25     97 IKEKDGKLVTKGDKGENGSSTDEGEGLVTAKEVIDAVNKAGWRMKTITAN 146
      *****

SEQ ID NO 35    201 GQTGQADKFETVTSGTNVTFASGKGTTATVSKDDQGNITVMYDVNVGDAL 250
SEQ ID NO 25    147 GQTGQADKFETVTSGTNVTFASGKGTTATVSKDDQGNITVMYDVNVGDAL 196
      *****

SEQ ID NO 35    251 NVNQLQNSGWNLDSKAVAGSSGKVISGNVSPSKGKMDETVNINAGNNIEI 300
SEQ ID NO 25    197 NVNQLQNSGWNLDSKAVAGSSGKVISGNVSPSKGKMDETVNINAGNNIEI 246
      *****

SEQ ID NO 35    301 TRNGKNIDIATSMTPQFSSVSLGAGADAPTLSDGDALNVGSKKDNKPVR 350
SEQ ID NO 25    247 TRNGKNIDIATSMTPQFSSVSLGAGADAPTLSDGDALNVGSKKDNKPVR 296
      *****

SEQ ID NO 35    351 ITNVAPGVKEGDVTNVAQLKGVAQNLNNRIDNVDGNARAGIAQAIATAGL 400
SEQ ID NO 25    297 ITNVAPGVKEGDVTNVAQLKGVAQNLNNRIDNVDGNARAGIAQAIATAGL 346
      *****

SEQ ID NO 35    401 VQAYLPGKSMMMAIGGGTYRGEAGYAIGYSSISDGGNWIIGKTASGNSRGH 450
SEQ ID NO 25    347 VQAYLPGKSMMMAIGGGTYRGEAGYAIGYSSISDGGNWIIGKTASGNSRGH 396
      *****

SEQ ID NO 35    451 FGASASVG YQW 461
SEQ ID NO 25    397 FGASASVG YQW 407
      *****
```


of 1

ClustalW (v1.4) multiple sequence alignment

2 Sequences Aligned Alignment Score = 2264
Gaps Inserted = 2 Conserved Identities = 391

Pairwise Alignment Mode: Slow
Pairwise Alignment Parameters:
 Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1
 Similarity Matrix: id

Multiple Alignment Parameters:
 Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1
 Delay Divergent = 40% Gap Distance = 8
 Similarity Matrix: id

Processing time: 0.3 seconds

1. SEQ ID NO 35 vs. SEQ ID NO 26

Aligned Length = 473 Gaps = 2
Identities = 391 (84%) Similarities = 4 (0%)

```
SEQ ID NO 35      1      NNETDLTSVGTEKLSFSANGNKVNITS DTKGLNFAKET  38
SEQ ID NO 26      1 MNKIYRIIWNALNAWVVVSELTRNHTKRAS--ATVKTAVLATLLFATVQ  48
                      *   *   *   *   *   *   *   *   *   *
                      *   *   *   *   *   *   *   *   *   *

SEQ ID NO 35     39 AGTNGD TTVHLNGIGSTLTDTLLNTGATTNVTNDNVT DDEKKRAASVKDV  88
SEQ ID NO 26     49 ASAN-----RAASVKDV  60
                      *   *   *   *   *   *   *   *   *   *

SEQ ID NO 35     89 LNAGWNIKGVKPGTTASDNVDFVRTYDTVEFLSADTKTTTVNVESKDNGK 138
SEQ ID NO 26     61 LNAGWNIKGVKPGTTASDNVDFVRTYDTVEFLSADTKTTTVNVESKDNGK 110
                      *****

SEQ ID NO 35    139 KTEVKIGAKTSVIKEKDGLVTGKDKGENSSSTDEGEGLVTAKEVIDAVN 188
SEQ ID NO 26    111 KTEVKIGAKTSVIKEKDGLVTGKDKGENSSSTDEGEGLVTAKEVIDAVN 160
                      *****

SEQ ID NO 35    189 KAGWRMKTTTANGQTGQADKFETVTS GNTVTFASGKGTTATVSKDDQGN I 238
SEQ ID NO 26    161 KAGWRMKTTTANGQTGQADKFETVTS GNTVTFASGKGTTATVSKDDQGN I 210
                      *****

SEQ ID NO 35    239 TVMYDVNVGDALNVNQLQNSGWNLDSKAVAGSSGKVISGNVSPSKGKMDE 288
SEQ ID NO 26    211 TVMYDVNVGDALNVNQLQNSGWNLDSKAVAGSSGKVISGNVSPSKGKMDE 260
                      *****

SEQ ID NO 35    289 TVNINAGNNIEITRNGKNIDIATSMTPQFSSVSLGAGADAP TLSVDGDAL 338
SEQ ID NO 26    261 TVNINAGNNIEITRNGKNIDIATSMTPQFSSVSLGAGADAP TLSVDGDAL 310
                      *****

SEQ ID NO 35    339 NVGSKKDNKPV RITNVAPGVKEGDVTNVAQLKGVAQNLNNRIDNVDGNAR 388
SEQ ID NO 26    311 NVGSKKDNKPV RITNVAPGVKEGDVTNVAQLKGVAQNLNNRIDNVDGNAR 360
                      *****

SEQ ID NO 35    389 AGIAQAIATAGLVQAYLP GKSMMAIGGGTYRGEAGYAIGYSSISDGGNWI 438
SEQ ID NO 26    361 AGIAQAIATAGLVQAYLP GKSMMAIGGGTYRGEAGYAIGYSSISDGGNWI 410
                      *****

SEQ ID NO 35    439 IKGTASGNSRGHFGASASVGYQW 461
SEQ ID NO 26    411 IKGTASGNSRGHFGASASVGYQW 433
                      *****
```

42

ClustalW (v1.4) multiple sequence alignment

2 Sequences Aligned Alignment Score = 2518
Gaps Inserted = 2 Conserved Identities = 429

Pairwise Alignment Mode: Slow

Pairwise Alignment Parameters:

Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1

Similarity Matrix: id

Multiple Alignment Parameters:

Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1

Delay Divergent = 40% Gap Distance = 8

Similarity Matrix: id

Processing time: 0.3 seconds

1. SEQ ID NO 35 vs. SEQ ID NO 27

Aligned Length = 531 Gaps = 2
Identities = 429 (85%) Similarities = 0 (0%)

```
SEQ ID NO 35      1
SEQ ID NO 27      1 MNKIYRIIWSALNAWVVVSELTRNHTKRASATVKTAVLATLLFATVQAS 50

SEQ ID NO 35      1
SEQ ID NO 27      51 ANTLKAGDNLKIKQFTYSLKKDLTDLTSVGTEKLSFSANGNKNVITS DTK 30
                      ***** 100

SEQ ID NO 35      31 GLNFAKETAGTNGDTTVHLNGIGSTLTDLLNTGATTNVTDNDVTDDEKK 80
SEQ ID NO 27      101 GLNFAKETAGTNGDTTVHLNGIGSTLTD----- 128
                      *****

SEQ ID NO 35      81 RAASVKDVLNAGWNIKGVPKGTASDNVDFVRTYDTVEFLSADTKTTTVN 130
SEQ ID NO 27      129 RAASVKDVLNAGWNIKGVK-----NVDFVRTYDTVEFLSADTKTTTVN 171
                      *****

SEQ ID NO 35      131 VESKDNGKKTEVKIGAKTSVIKEKDGLVTGKDKGENGSSTDEGEGLVTA 180
SEQ ID NO 27      172 VESKDNGKKTEVKIGAKTSVIKEKDGLVTGKDKGENGSSTDEGEGLVTA 221
                      *****

SEQ ID NO 35      181 KEVIDAVNKAGWRMKT TTTANGQTGQADKFETVTS GNTVTFASGKGTTATV 230
SEQ ID NO 27      222 KEVIDAVNKAGWRMKT TTTANGQTGQADKFETVTS GNTVTFASGKGTTATV 271
                      *****

SEQ ID NO 35      231 SKDDQGNITVMYDVNVGDALNVNQLQNSGWNLDSKAVAGSSGKVISGNVS 280
SEQ ID NO 27      272 SKDDQGNITVMYDVNVGDALNVNQLQNSGWNLDSKAVAGSSGKVISGNVS 321
                      *****

SEQ ID NO 35      281 PSKGKMDETVNINAGNNIEITRNGKNIDIATSMTPQFSSVSLGAGADAPT 330
SEQ ID NO 27      322 PSKGKMDETVNINAGNNIEITRNGKNIDIATSMTPQFSSVSLGAGADAPT 371
                      *****

SEQ ID NO 35      331 LSV DGDALNVGSKKDNKPV RITNVAPGVKEGDVTNVAQLKGVAQNLNNRI 380
SEQ ID NO 27      372 LSV DGDALNVGSKKDNKPV RITNVAPGVKEGDVTNVAQLKGVAQNLNNRI 421
                      *****

SEQ ID NO 35      381 DNVDGNARAGIAQAIATAGLVQAYLPGKSMM AIGGGTYRGEAGYAIGYSS 430
SEQ ID NO 27      422 DNVDGNARAGIAQAIATAGLVQAYLPGKSMM AIGGGTYRGEAGYAIGYSS 471
                      *****
```

of 2

```
SEQ ID NO 35 431 ISDGGNWIIGKTASGNSRGHFGASASVGYQW 461
SEQ ID NO 27 472 ISDGGNWIIGKTASGNSRGHFGASASVGYQW 502
*****
```

of 1

ClustalW (v1.4) multiple sequence alignment

2 Sequences Aligned Alignment Score = 2544
Gaps Inserted = 1 Conserved Identities = 440

Pairwise Alignment Mode: Slow

Pairwise Alignment Parameters:

Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1
Similarity Matrix: id

Multiple Alignment Parameters:

Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1
Delay Divergent = 40% Gap Distance = 8
Similarity Matrix: id

Processing time: 0.3 seconds

1. SEQ ID NO 35 vs. SEQ ID NO 36

Aligned Length = 462 Gaps = 1
Identities = 440 (95%) Similarities = 1 (0%)

```
SEQ ID NO 35   1 NNETDLTSVGTEKLSFSANGNKVNITSDTKGLNFAKETAGTNGDTTVHLN  50
SEQ ID NO 36   1 TDETGLINVETEKLSFGANGKKVNIISDTKGLNFAKETAGTNGDTTVHLN  50
               * * * * *
               *****

SEQ ID NO 35   51 GIGSTLTDTLLNTGATTNVTNDNVTDDDEKKRAASVKDVLNAGWNIKGVPK 100
SEQ ID NO 36   51 GIGSTLTDMLLNTGATTNVTNDNVTDDDEKKRAASVKDVLNAGWNIKGVPK 100
               *****

SEQ ID NO 35   101 GTTASDNVDFVRTYDTVEFLSADTKTTTVNVESKDNGKKTEVKIGAKTSV 150
SEQ ID NO 36   101 GTTASDNVDFVRTYDTVEFLSADTKTTTVNVESKDNGKKTEVKIGAKTSV 150
               *****

SEQ ID NO 35   151 IKEKDGLVLTGKDKGENGSSTDEGEGLVTAKEVIDAVNKAGWRMKTITAN 200
SEQ ID NO 36   151 IKEKDGLVLTGKDKGENGSSTDEGEGLVTAKEVIDAVNKAGWRMKTITAN 200
               *****

SEQ ID NO 35   201 GQTGQADKFETVTSGTNVTFASGKGTATVSKDDQGNITVMYDVNVGDAL  250
SEQ ID NO 36   201 GQTGQADKFETVTSGTKVTFASGNGTTATVSKDDQGNITVKYDVNVGDAL  250
               *****

SEQ ID NO 35   251 NVNQLQNSGWNLDSKAVAGSSGKVISGNVSPSKGKMDETVNINAGNNIEI  300
SEQ ID NO 36   251 NVNQLQNSGWNLDSKAVAGSSGKVISGNVSPSKGKMDETVNINAGNNIEI  300
               *****

SEQ ID NO 35   301 TRNGKNIDIATSMTPQFSSVSLGAGADAPTLSDVG-DALNVGSKKDNKPV  349
SEQ ID NO 36   301 TRNGKNIDIATSMTPQFSSVSLGAGADAPTLSDVDEGALNVGSKDANKPV  350
               *****

SEQ ID NO 35   350 RITNVAPGVKEGDVTNVAQLKGVAQNLNNRIDNVNGNARAGIAQAIATAG  399
SEQ ID NO 36   351 RITNVAPGVKEGDVTNVAQLKGVAQNLNNRIDNVNGNARAGIAQAIATAG  400
               *****

SEQ ID NO 35   400 LVQAYLPGKSMMAIGGGTYLGEAGYAIGYSSISDGGNWIIGKTASGNSRG  449
SEQ ID NO 36   401 LVQAYLPGKSMMAIGGGTYLGEAGYAIGYSSISAGGNWIIGKTASGNSRG  450
               *****

SEQ ID NO 35   450 HFGASASVGYQW  461
SEQ ID NO 36   451 HFGASASVGYQW  462
               *****
```

of 1

ClustalW (v1.4) multiple sequence alignment

2 Sequences Aligned Alignment Score = 2075
Gaps Inserted = 0 Conserved Identities = 355

Pairwise Alignment Mode: Slow

Pairwise Alignment Parameters:

Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1
Similarity Matrix: id

Multiple Alignment Parameters:

Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1
Delay Divergent = 40% Gap Distance = 8
Similarity Matrix: id

Processing time: 0.3 seconds

1. SEQ ID NO 35 vs. SEQ ID NO 37

Aligned Length = 461 Gaps = 0
Identities = 355 (77%) Similarities = 0 (0%)

```
SEQ ID NO 35   1 NNETDLTSVGTEKLSFSANGNKVNITSDTKGLNFAKETAGTNGDTTVHLN  50
SEQ ID NO 37   1                                     0

SEQ ID NO 35  51 GIGSTLTDTLLNTGATTNVTNDNVTDDEKKRAASVKDVLNAGWNIKGVPK 100
SEQ ID NO 37   1                                     0

SEQ ID NO 35 101 GTTASDNVDFVRTYDTVEFLSADTKTTTVNVESKDNGKKTEVKIGAKTSV 150
SEQ ID NO 37   1      NNVDFVRTYDTVEFLSADTKTTTVNVESKDNGKKTEVKIGAKTSV  45
                *****

SEQ ID NO 35 151 IKEKDGLVLTGKDKGENGSSTDEGEGLVTAKEVIDAVNKAGWRMKTITAN 200
SEQ ID NO 37  46 IKEKDGLVLTGKDKGENGSSTDEGEGLVTAKEVIDAVNKAGWRMKTITAN  95
                *****

SEQ ID NO 35 201 GQTGQADKFETVTSGTNVTFASGKGTATVSKDDQGNITVMYDVNVGDAL 250
SEQ ID NO 37  96 GQTGQADKFETVTSGTNVTFASGKGTATVSKDDQGNITVMYDVNVGDAL 145
                *****

SEQ ID NO 35 251 NVNQLQNSGWNLDSKAVAGSSGKVISGNVSPSKGKMDETVNINAGNNIEI 300
SEQ ID NO 37 146 NVNQLQNSGWNLDSKAVAGSSGKVISGNVSPSKGKMDETVNINAGNNIEI 195
                *****

SEQ ID NO 35 301 TRNGKNIDIATSMTPQFSSVSLGAGADAPTLSVDGDALNVGSKKDNKPVR 350
SEQ ID NO 37 196 TRNGKNIDIATSMTPQFSSVSLGAGADAPTLSVDGDALNVGSKKDNKPVR 245
                *****

SEQ ID NO 35 351 ITNVAPGVKEGDVTNVAQLKGVAQNLNLRIDNVDGNARAGIAQAIATAGL 400
SEQ ID NO 37 246 ITNVAPGVKEGDVTNVAQLKGVAQNLNLRIDNVDGNARAGIAQAIATAGL 295
                *****

SEQ ID NO 35 401 VQAYLPGKSMMAIGGGTYRGEAGYAIGYSSISDGGNWIIGKTASGNSRGH 450
SEQ ID NO 37 296 VQAYLPGKSMMAIGGGTYRGEAGYAIGYSSISDGGNWIIGKTASGNSRGH 345
                *****

SEQ ID NO 35 451 FGASASVGYQW 461
SEQ ID NO 37 346 FGASASVGYQW 356
                *****
```

ClustalW (v1.4) multiple sequence alignment

2 Sequences Aligned Alignment Score = 2229
Gaps Inserted = 0 Conserved Identities = 381

Pairwise Alignment Mode: Slow

Pairwise Alignment Parameters:

Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1
Similarity Matrix: id

Multiple Alignment Parameters:

Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1
Delay Divergent = 40% Gap Distance = 8
Similarity Matrix: id

Processing time: 0.3 seconds

1. SEQ ID NO 35 vs. SEQ ID NO 38

Aligned Length = 461 Gaps = 0
Identities = 381 (82%) Similarities = 0 (0%)

```
SEQ ID NO 35   1 NNETDLTSVGTEKLSFSANGNKVNITSDTKGLNFAKETAGTNGDTTVHLN   50
SEQ ID NO 38   1                                     0

SEQ ID NO 35   51 GIGSTLTDTLLNTGATTNVTNDNVTDDEKKRAASVKDVLNAGWNIKGVPK 100
SEQ ID NO 38   1                                     NRAASVKDVLNAGWNIKGVPK 21
                                     *****

SEQ ID NO 35  101 GTTASDNVDFVRTYDTVEFLSADTKTTTVNVESKDNGKKTEVKIGAKTSV 150
SEQ ID NO 38  22 GTTASDNVDFVRTYDTVEFLSADTKTTTVNVESKDNGKKTEVKIGAKTSV 71
                                     *****

SEQ ID NO 35  151 IKEKDGKLVTKDKGGENGSSTDEGEGLVTAKEVIDAVNKAGWRMKTITAN 200
SEQ ID NO 38  72 IKEKDGKLVTKDKGGENGSSTDEGEGLVTAKEVIDAVNKAGWRMKTITAN 121
                                     *****

SEQ ID NO 35  201 GQTGGQADKFETVTSNTVTFASGKGTATVSKDDQGNITVMYDVNVGDAL 250
SEQ ID NO 38  122 GQTGGQADKFETVTSNTVTFASGKGTATVSKDDQGNITVMYDVNVGDAL 171
                                     *****

SEQ ID NO 35  251 NVNQLQNSGWNLDSKAVAGSSGKVISGNVSPSKGKMDETVNINAGNNIEI 300
SEQ ID NO 38  172 NVNQLQNSGWNLDSKAVAGSSGKVISGNVSPSKGKMDETVNINAGNNIEI 221
                                     *****

SEQ ID NO 35  301 TRNGKNIDIATSMTPQFSSVSLGAGADAPTLSDGDALNVGSKKDNKPVR 350
SEQ ID NO 38  222 TRNGKNIDIATSMTPQFSSVSLGAGADAPTLSDGDALNVGSKKDNKPVR 271
                                     *****

SEQ ID NO 35  351 ITNVAPGVKEGDVTNVAQLKGVAQNLNNRIDNVDGNARAGIAQAIATAGL 400
SEQ ID NO 38  272 ITNVAPGVKEGDVTNVAQLKGVAQNLNNRIDNVDGNARAGIAQAIATAGL 321
                                     *****

SEQ ID NO 35  401 VQAYLPGKSMMAIGGGTYRGEAGYAIGYSSISDGGNWIKGTASGNSRGH 450
SEQ ID NO 38  322 VQAYLPGKSMMAIGGGTYRGEAGYAIGYSSISDGGNWIKGTASGNSRGH 371
                                     *****

SEQ ID NO 35  451 FGASASVGYQW 461
SEQ ID NO 38  372 FGASASVGYQW 382
                                     *****
```

41

ClustalW (v1.4) multiple sequence alignment

2 Sequences Aligned Alignment Score = 2518
Gaps Inserted = 2 Conserved Identities = 429

Pairwise Alignment Mode: Slow

Pairwise Alignment Parameters:

Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1
Similarity Matrix: id

Multiple Alignment Parameters:

Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1
Delay Divergent = 40% Gap Distance = 8
Similarity Matrix: id

Processing time: 0.3 seconds

1. SEQ ID NO 35 vs. SEQ ID NO 39

Aligned Length = 482 Gaps = 2
Identities = 429 (93%) Similarities = 0 (0%)

```
SEQ ID NO 35      1                      NNETDLTSVGTEKLSFSANGNKVNITSDT 29
SEQ ID NO 39      1 SANTLKAGDNLKIKQFTYSLKKDLTDLTSVGTEKLSFSANGNKVNITSDT 50
                      *****

SEQ ID NO 35     30 KGLNFAKETAGTNGDTTVHLNGIGSTLTDTLLNTGATTNVTNDNVTDDEK 79
SEQ ID NO 39     51 KGLNFAKETAGTNGDTTVHLNGIGSTLTD----- 79
                      *****

SEQ ID NO 35     80 KRAASVKDVLNAGWNIKGVKPGTTASDNVDFVRTYDTVEFLSADTKTTTV 129
SEQ ID NO 39     80 -RAASVKDVLNAGWNIKGVK-----NVDFVRTYDTVEFLSADTKTTTV 121
                      *****

SEQ ID NO 35    130 NVESKDNGKKTEVKIGAKTSVIKEKDGLVTGKDKGENGSSTDEGEGLVT 179
SEQ ID NO 39    122 NVESKDNGKKTEVKIGAKTSVIKEKDGLVTGKDKGENGSSTDEGEGLVT 171
                      *****

SEQ ID NO 35    180 AKEVIDAVNKAGWRMKTITANGQTGQADKFETVTSNTVTFASGKGTTAT 229
SEQ ID NO 39    172 AKEVIDAVNKAGWRMKTITANGQTGQADKFETVTSNTVTFASGKGTTAT 221
                      *****

SEQ ID NO 35    230 VSKDDQGNITVMYDVNVGDALNVNQLQNSGWNLDSKAVAGSSGKVISGNV 279
SEQ ID NO 39    222 VSKDDQGNITVMYDVNVGDALNVNQLQNSGWNLDSKAVAGSSGKVISGNV 271
                      *****

SEQ ID NO 35    280 SPSKGKMDETVNINAGNNIEITRNGKNIDIATSMTPQFSSVSLGAGADAP 329
SEQ ID NO 39    272 SPSKGKMDETVNINAGNNIEITRNGKNIDIATSMTPQFSSVSLGAGADAP 321
                      *****

SEQ ID NO 35    330 TLSVDGDALNVGSKKDNKPVRIITNVAPGVKEGDVTNVAQLKGVAQNLNNR 379
SEQ ID NO 39    322 TLSVDGDALNVGSKKDNKPVRIITNVAPGVKEGDVTNVAQLKGVAQNLNNR 371
                      *****

SEQ ID NO 35    380 IDNVDGNARAGIAQAIATAGLVQAYLPGKSMMIAIGGGTYRGEAGYAIGYS 429
SEQ ID NO 39    372 IDNVDGNARAGIAQAIATAGLVQAYLPGKSMMIAIGGGTYRGEAGYAIGYS 421
                      *****

SEQ ID NO 35    430 SISDGGNWIIGKTASGNSRGHFGASASVGYQW 461
SEQ ID NO 39    422 SISDGGNWIIGKTASGNSRGHFGASASVGYQW 453
                      *****
```

SEQUENCE COMPARISONS Massignani WO99/36544 vs. US App. 09/771,382

A: Peak US 6,197,312 SEQ ID NO:2 = SEQ ID NO:4 of Massignani

MNKIYRIIWN	SALNAWVVVS	ELTRNHTKRA	SATVKTAVLA	TLLFATVQAS	ANNEEQEEDL	60
YLDPVQRTVA	VLIVNSDKEG	TGEKEKVEEN	SDWAVYFNEK	GVLTAAREITL	KAGDNLKIKQ	120
NGTNFTYSLK	KDLTDLTSVG	TEKLSFSANG	NKVNITSDTK	GLNFAKETAG	TNGDTTVHLN	180
GIGSTLTDTL	LNTGATTNVT	NDNVTDDDEK	RAASVKDVLN	AGWNIKGVPK	GTTASDNVDF	240
VRTYDTVEFL	SADTKTTTVN	VESKDNGKKT	EVKIGAKTSV	IKEKDGKLV	GKDKGENGSS	300
TDEGEGLVTA	KEVIDAVNKA	GWRMKT'TAN	GQTGQADKFE	TVTSGTNVTF	ASGKGTTATV	360
SKDDQGNITV	MYDVNVGDAL	NVNQLQNSGW	NLDSKAVAGS	SGKVISGNVS	PSKKGKMDTV	420
NINAGNNIEI	TRNGKNIDIA	TSMTPOFSSV	SLGAGADAPT	LSVDGDALNV	GSKKDNKPVR	480
ITNVAPGVKE	GDVTNVAQLK	GVAQNLNNRI	DNVDGNARAG	IAQAIATAGL	VQAYLPGKSM	540
MAIGGGTYRG	EAGYAIGYSS	ISDGGNWIIK	GTASGNSRGH	FGASASVGYQ	W	591

B: SEQ ID NO:23 of US App. 09/771,382

MNKIYRIIWN	SALNAWVVVS	ELTRNHTKRA	SATVKTAVLA	TLLFATVQAS	ANNETDLTSV	60
GTEKLSFSAN	GNKVNITSDT	KGLNFAKETA	GTNGDTTVHL	NGIGSTLTDT	LLNTGATTNV	120
TNDNVTDDDEK	KRAASVKDVL	NAGWNIKGVPK	PGTTASDNVD	FVRTYDTVEF	LSADTKTTTV	180
NVESKDNGKK	TEVKIGAKTS	VIKEKDGKLV	TGKDKGENGS	STDEGEGLVT	AKEVIDAVNK	240
AGWRMKT'TTA	NGQTGQADKF	ETVTSGTNVT	FASGKGTTAT	VSKDDQGNIT	VMYDVNVGDA	300
LVNVLQNSG	WNLSKAVAG	SSGKVISGNV	SPSKGKMDTV	VNINAGNNIE	ITRNGKNIDI	360
ATSMTPQFSS	VSLGAGADAP	TLSVDGDALN	VGSKKDNKPV	RITNVAPGVK	EGDVTNVAQL	420
KGVAQNLNNR	IDNVDGNARA	GIAQAIATAG	LVQAYLPGKS	MMAIGGGTYR	GEAGYAIGYS	480
SISDGGNWII	KGTASGNSRG	HFGASASVGY	QW			

C: SEQ ID NO:35 of US App. 09/771,382

NNETDLTSVG	TEKLSFSANG	NKVNITSDTK	GLNFAKETAG	TNGDTTVHLN	GIGSTLTDTL	60
LNTGATTNVT	NDNVTDDDEK	RAASVKDVLN	AGWNIKGVPK	GTTASDNVDF	VRTYDTVEFL	120
SADTKTTTVN	VESKDNGKKT	EVKIGAKTSV	IKEKDGKLV	GKDKGENGSS	TDEGEGLVTA	180
KEVIDAVNKA	GWRMKT'TAN	GQTGQADKFE	TVTSGTNVTF	ASGKGTTATV	SKDDQGNITV	240
MYDVNVGDAL	NVNQLQNSGW	NLDSKAVAGS	SGKVISGNVS	PSKKGKMDTV	NINAGNNIEI	300
TRNGKNIDIA	TSMTPOFSSV	SLGAGADAPT	LSVDGDALNV	GSKKDNKPVR	ITNVAPGVKE	360
GDVTNVAQLK	GVAQNLNNRI	DNVDGNARAG	IAQAIATAGL	VQAYLPGKSM	MAIGGGTYRG	420
EAGYAIGYSS	ISDGGNWIIK	GTASGNSRGH	FGASASVGYQ	W		

Run comparisons to determine % identity:

B vs A

C vs A

Alignments carried out using "clustalW".

ClustalW (v1.4) multiple sequence alignment

ClustalW (v1.4) multiple sequence alignment

2 Sequences Aligned Alignment Score = 2976

Gaps Inserted = 1 Conserved Identities = 512

Pairwise Alignment Mode: Slow

Pairwise Alignment Parameters:

Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1

Similarity Matrix: id

Multiple Alignment Parameters:

Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1

Delay Divergent = 40% Gap Distance = 8

Similarity Matrix: id

Processing time: 0.7 seconds

```
B   1 MNKIYRIIWNSALNAWVVVSELTRNHTKRASATVKTAVLATLLFATVQAS   50
A   1 MNKIYRIIWNSALNAWVVVSELTRNHTKRASATVKTAVLATLLFATVQAS   50
    *****

B   51 ANNE----- 54
A   51 ANNEEQEEDLYLDPVQRTVAVLIVNSDKEGTGEKEKVEENS DWAVYFNEK 100
    ****

B   55 -----TDLTSVGTEKLSFSANG 71
A  101 GVLTAAREITLKAGDNLKIKQNGTNFTYSLKKDLTDLTSVGTEKLSFSANG 150
    *****

B   72 NKVNITSDTKGLNFAKETAGTNGDTTVHLNGIGSTLTDLLNTGATTNVT 121
A  151 NKVNITSDTKGLNFAKETAGTNGDTTVHLNGIGSTLTDLLNTGATTNVT 200
    *****

B  122 NDNVTDEKKRAASVKDVLNAGWNIKGVP GTTASDNVDFVRTYDTVEFL 171
A  201 NDNVTDEKKRAASVKDVLNAGWNIKGVP GTTASDNVDFVRTYDTVEFL 250
    *****

B  172 SADTKTTTVNVESKDNGKKTEVKIGAKTSVIKEKDGLVTGKDKGENGSS 221
A  251 SADTKTTTVNVESKDNGKKTEVKIGAKTSVIKEKDGLVTGKDKGENGSS 300
    *****

B  222 TDEGEGLVTAKEVIDAVNKAGWRMKT TTTANGQTGQADKFETVTSGTNVTF 271
A  301 TDEGEGLVTAKEVIDAVNKAGWRMKT TTTANGQTGQADKFETVTSGTNVTF 350
```

```

*****
B 272 ASGKGTTATVSKDDQGNITVMYDVNVGDALNVNQLQNSGWNLDKAVAGS 321
A 351 ASGKGTTATVSKDDQGNITVMYDVNVGDALNVNQLQNSGWNLDKAVAGS 400
*****

B 322 SGKVISGNVSPSKGKMDETVNINAGNNIEITRNGKNIDIATSMTPQFSSV 371
A 401 SGKVISGNVSPSKGKMDETVNINAGNNIEITRNGKNIDIATSMTPQFSSV 450
*****

B 372 SLGAGADAPTLSVDGDALNVGSKKDNKPVRITNVAPGVKEGDVTNVAQLK 421
A 451 SLGAGADAPTLSVDGDALNVGSKKDNKPVRITNVAPGVKEGDVTNVAQLK 500
*****

B 422 GVAQNLNNRIDNVDGNARAGIAQAIATAGLVQAYLPGKSMMMAIGGGTYRG 471
A 501 GVAQNLNNRIDNVDGNARAGIAQAIATAGLVQAYLPGKSMMMAIGGGTYRG 550
*****

B 472 EAGYAIGYSSISDGGNWIICKGTASGNSRGHFGASASVGYQW 512
A 551 EAGYAIGYSSISDGGNWIICKGTASGNSRGHFGASASVGYQW 591
*****

```

% identity = 512 conserved identities/591 amino acids = 86.6%

Option 1 (no gaps in C)
ClustalW (v1.4) multiple sequence alignment

2 Sequences Aligned Alignment Score = 2663
Gaps Inserted = 0 Conserved Identities = 458

Pairwise Alignment Mode: Slow

Pairwise Alignment Parameters:

Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1

Similarity Matrix: id

Multiple Alignment Parameters:

Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1

Delay Divergent = 40% Gap Distance = 8

Similarity Matrix: id

Processing time: 0.6 seconds

1. C vs. A

Aligned Length = 591 Gaps = 0
Identities = 458 (77%) Similarities = 0 (0%)

```

C   1  ----- 0
A   1 MNKIYRIIWSALNAWVVVSELTRNHTKRASATVKTAVLATLLFATVQAS 50

C   1  ----- 0
A  51 ANNEEQEEDLYLDPVQRTVAVLIVNSDKEGTGEKEKVEENS DWAVYFNEK 100

C   1  -----NNETDLTSVGTEKLSFSANG 20
A 101 GVLTA REITLKAGDNLKIKQNGTNFTYSLKKDLTDLTSVGTEKLSFSANG 150
      *****

C   21 NKNVITS DTKGLNFAKETAGTNGD TTVHLNGIGSTLTDTLLNTGATTNVT 70
A 151 NKNVITS DTKGLNFAKETAGTNGD TTVHLNGIGSTLTDTLLNTGATTNVT 200
      *****

C   71 NDNVTDDEKKRAASVKDVLNAGWNIKGVP GTTASDNVDFVRTYDTVEFL 120
A 201 NDNVTDDEKKRAASVKDVLNAGWNIKGVP GTTASDNVDFVRTYDTVEFL 250
      *****

C  121 SADTKTTTVNVESKDNGKKTEVKIGAKTSVIKEKDGLVTGKDKGENGSS 170
A 251 SADTKTTTVNVESKDNGKKTEVKIGAKTSVIKEKDGLVTGKDKGENGSS 300
      *****

C  171 TDEGEGLVTAKEVIDAVNKAGWRMKT T TANGQTGQADKFETVTSGTNVTF 220
A 301 TDEGEGLVTAKEVIDAVNKAGWRMKT T TANGQTGQADKFETVTSGTNVTF 350
      *****

C  221 ASGKGTTATVSKDDQGNITVMYDVNVGDALNVNQLQNSGWNLDSKAVAGS 270
A 351 ASGKGTTATVSKDDQGNITVMYDVNVGDALNVNQLQNSGWNLDSKAVAGS 400

```

```

*****

C 271 SGKVISGNVSPSKGKMDETVNINAGNNIEITRNGKNIDIATSMTPQFSSV 320
A 401 SGKVISGNVSPSKGKMDETVNINAGNNIEITRNGKNIDIATSMTPQFSSV 450
*****

C 321 SLGAGADAPTLSVDGDALNVGSKKDNKPVRLTNVAPGVKEGDVTNVAQLK 370
A 451 SLGAGADAPTLSVDGDALNVGSKKDNKPVRLTNVAPGVKEGDVTNVAQLK 500
*****

C 371 GVAQNLNNRIDNVDGNARAGIAQAIATAGLVQAYLPGKSMMMAIGGGTYRG 420
A 501 GVAQNLNNRIDNVDGNARAGIAQAIATAGLVQAYLPGKSMMMAIGGGTYRG 550
*****

C 421 EAGYAIGYSSISDGGNWIICKGTASGNSRGHFGASASVGYQW 461
A 551 EAGYAIGYSSISDGGNWIICKGTASGNSRGHFGASASVGYQW 591
*****

```

Option 2 (manual alignment, gap in C
ClustalW (v1.4) multiple sequence alignment

2 Sequences Aligned Alignment Score = 2691
Gaps Inserted = 1 Conserved Identities = 461

Pairwise Alignment Mode: Slow

Pairwise Alignment Parameters:

Open Gap Penalty = 10.0 Extend Gap Penalty = 0.2

Similarity Matrix: id

Multiple Alignment Parameters:

Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1

Delay Divergent = 40% Gap Distance = 8

Similarity Matrix: id

Processing time: 0.6 seconds

1. C vs. A

Aligned Length = 591 Gaps = 1
Identities = 461 (78%) Similarities = 0 (0%)

```

C   1  ----- 0
A   1  MNKIYRIIWNALNAWVVSELTRNHTKRASATVKTAVLATLLFATVQAS 50

C   1  -NNE----- 3
A  51  ANNEEQEEDLYLDPVQRTVAVLIVNSDKEGTGEKEKVEENSDWAVYFNEK 100
      ***

C   4  -----TDLTSVGTEKLSFSANG 20
A  101  GVLTAREITLKAGDNLKIKQNGTNFTYSLKDLTDLTSVGTEKLSFSANG 150
      *****

C  21  NKVNITSDTKGLNFAKETAGTNGDTTVHLNGIGSTLTDLLNTGATTNVT 70
A  151  NKVNITSDTKGLNFAKETAGTNGDTTVHLNGIGSTLTDLLNTGATTNVT 200
      *****

C  71  NDNVTDDEKKRAASVKDVLNAGWNIKGVPGTTASDNVDFVRTYDTVEFL 120
A  201  NDNVTDDEKKRAASVKDVLNAGWNIKGVPGTTASDNVDFVRTYDTVEFL 250
      *****

C  121  SADTKTTTVNVESKDNGKKTEVKIGAKTSVIKEKDGLVTGKDKGENGSS 170
A  251  SADTKTTTVNVESKDNGKKTEVKIGAKTSVIKEKDGLVTGKDKGENGSS 300
      *****

C  171  TDEGEGLVTAKEVIDAVNKAGWRMKT TTANGQTGQADKFETVTS GTNVTF 220
A  301  TDEGEGLVTAKEVIDAVNKAGWRMKT TTANGQTGQADKFETVTS GTNVTF 350
      *****

C  221  ASGKGTTATVSKDDQGNITVMYDVNVGDALNVNQLQNSGWNLDSKAVAGS 270
A  351  ASGKGTTATVSKDDQGNITVMYDVNVGDALNVNQLQNSGWNLDSKAVAGS 400
      *****

```

C 271 SGKVISGNVSPSKGKMDETVDNINAGNNIEITRNGKNIDIATSMTPQFSSV 320
 A 401 SGKVISGNVSPSKGKMDETVDNINAGNNIEITRNGKNIDIATSMTPQFSSV 450

 C 321 SLGAGADAPTLSVDGDALNVGSKKDNKPVRITNVAPGVKEGDVTNVAQLK 370
 A 451 SLGAGADAPTLSVDGDALNVGSKKDNKPVRITNVAPGVKEGDVTNVAQLK 500

 C 371 GVAQNLNNRIDNVDGNARAGIAQAIATAGLVQAYLPGKSMMMAIGGGTYRG 420
 A 501 GVAQNLNNRIDNVDGNARAGIAQAIATAGLVQAYLPGKSMMMAIGGGTYRG 550

 C 421 EAGYAIGYSSISDGGNWI IKGTASGNSRGHFGASASVGYQW 461
 A 551 EAGYAIGYSSISDGGNWI IKGTASGNSRGHFGASASVGYQW 591

SEQUENCE COMPARISONS Peak US Patent 6,197,312 vs. US App. 09/771,382

Attached are documents that provide the sequences for alignment.

The purpose is:

- (a) to determine the % identity between Peak SEQ ID NO:2 and SEQ ID NO:23 &
- (b) to determine the % identity between Peak SEQ ID NO:2 and SEQ ID NO:35.

The determination should be over the entire length of each protein.

(a) = 86% (see attached pages 2 vs 23.pdf)

(b) = 77% (see attached pages 2 vs 35.pdf)

Peak US Patent 6,197,312 SEQ ID NO:2

MNKIYRIIWN	SALNAWVVVS	ELTRNHTKRA	SATVKTAFLA	TLLFATVQAS	ANNEPRPKKD	60
LYLDPVQRTV	AVLIVNSDKE	GTGEKEKVEE	NSDWAVYFNE	KGVLTAAREIT	KAGDNLKIKQ	120
NGTNFTYSLK	KDLTDLTSVG	TEKLSFSANG	NKVNITSDDK	GLNFAKETAG	TNGDITVHLN	180
GIGSTLTDTL	LNTGATTNVT	NDNVTDDDEK	RAASVKDVLN	AGWNIKGVPK	GTTASDNVDF	240
VRTYDTVEFL	SADTKTTTVN	VESKDNGKKT	EVKIGAKTSV	IKEKDGLVT	GKDKGENGSS	300
TDEGEGLVTA	KEVIDAVNKA	GWRMKTITAN	GQTQADKFE	TVTSGTNVTF	ASGKGTTATV	360
SKDDQGNITV	MYDVNVGDAL	NVNQLQNSGW	NLDSKAVAGS	SGKVISGNVS	PSKGKMDTV	420
NINAGNNIEI	TRNGKNIDIA	TSMTPQFSSV	SLGAGADAPT	LSVDGDALNV	GSKKDNKPVR	480
ITNVAPGVKE	GDVTNVAQLK	GVAQNLNNRI	DNVDGNARAG	IAQAIATAGL	VQAYLPGKSM	540
MAIGGGTYRG	EAGYAIGYSS	ISDGGNWIIC	GTASGNSRGH	FGASASVGYQ	W	

US App. 09/771,382 SEQ ID NO:23

MNKIYRIIWN	SALNAWVVVS	ELTRNHTKRA	SATVKTAFLA	TLLFATVQAS	ANNETDLTSV	60
GTEKLSFSAN	GNKVNITSDD	KGLNFAKETA	GTNGDITVHL	NGIGSTLTDT	LLNTGATTNV	120
TNDNVTDDDEK	KRAASVKDVL	NAGWNIKGVPK	PGTTASDNVD	FVRTYDTVEF	LSADTKTTTV	180
NVESKDNGKK	TEVKIGAKTS	VIKEKDGLVT	TGDKGENGSS	STDEGEGLVT	AKEVIDAVNK	240
AGWRMKTITTA	NGQTQADKFE	ETVTSNTVTF	FASGKGTTAT	VSKDDQGNIT	VMYDVNVGDA	300
LNVNQLQNSG	WNLDSKAVAG	SSGKVISGNV	SPSKGKMDTV	VNINAGNNIE	ITRNGKNIDI	360
ATSMTPQFSS	VSLGAGADAP	TLSDVDGDALN	VGSKKDNKPV	RITNVAPGVK	EGDVTNVAQL	420
KGVAQNLNNR	IDNVNVDGARA	GIAQAIATAG	LVQAYLPGKS	MMAIGGGTYR	GEAGYAIGYS	480
SISDGGNWIIC	KGTASGNSRG	HFGASASVGY	QW			

US App. 09/771,382 SEQ ID NO:35

NNETDLTSVG	TEKLSFSANG	NKVNITSDDK	GLNFAKETAG	TNGDITVHLN	GIGSTLTDTL	60
LNTGATTNVT	NDNVTDDDEK	RAASVKDVLN	AGWNIKGVPK	GTTASDNVDF	VRTYDTVEFL	120
SADTKTTTVN	VESKDNGKKT	EVKIGAKTSV	IKEKDGLVT	GKDKGENGSS	TDEGEGLVTA	180
KEVIDAVNKA	GWRMKTITAN	GQTQADKFE	TVTSGTNVTF	ASGKGTTATV	SKDDQGNITV	240
MYDVNVGDAL	NVNQLQNSGW	NLDSKAVAGS	SGKVISGNVS	PSKGKMDTV	NINAGNNIEI	300
TRNGKNIDIA	TSMTPQFSSV	SLGAGADAPT	LSVDGDALNV	GSKKDNKPVR	ITNVAPGVKE	360
GDVTNVAQLK	GVAQNLNNRI	DNVDGNARAG	IAQAIATAGL	VQAYLPGKSM	MAIGGGTYRG	420
EAGYAIGYSS	ISDGGNWIIC	GTASGNSRGH	FGASASVGYQ	W		

of 2

ClustalW (v1.4) multiple sequence alignment

2 Sequences Aligned Alignment Score = 2968
Gaps Inserted = 1 Conserved Identities = 511

Pairwise Alignment Mode: Slow
Pairwise Alignment Parameters:
 Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1
 Similarity Matrix: id

Multiple Alignment Parameters:
 Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1
 Delay Divergent = 40% Gap Distance = 8
 Similarity Matrix: id

Processing time: 0.3 seconds

1. SEQ ID 2 vs. SEQ ID 23

 Aligned Length = 592 Gaps = 1
 Identities = 511 (86%) Similarities = 0 (0%)

```
SEQ ID 2   1 MNKIYRIIWSALNAWVVVSELTRNHTKRASATVKTAVLATLLFATVQAS   50
SEQ ID 23  1 MNKIYRIIWSALNAWVVVSELTRNHTKRASATVKTAVLATLLFATVQAS   50
*****

SEQ ID 2   51 ANNERPRKKDLYLDPVQRTVAVLIVNSDKEGTGEKEKVEENS DWAVYFNE 100
SEQ ID 23  51 ANN----- 53
***

SEQ ID 2   101 KGVLTAREITLKAGDNLKIKQNGTNFTYSLKKDLTDLTSVGTEKLSFSAN 150
SEQ ID 23  54 -----ETDLTSVGTEKLSFSAN 70
*****

SEQ ID 2   151 GNKNVITS DTKGLNFAKETAGTNGD TTVHLNGIGSTLTD TLLNTGATTNV 200
SEQ ID 23  71 GNKNVITS DTKGLNFAKETAGTNGD TTVHLNGIGSTLTD TLLNTGATTNV 120
*****

SEQ ID 2   201 TNDNVT DDEKKRAASVKDVLNAGWNIKGVP GTTASDNVDFVRTYDTVEF 250
SEQ ID 23  121 TNDNVT DDEKKRAASVKDVLNAGWNIKGVP GTTASDNVDFVRTYDTVEF 170
*****

SEQ ID 2   251 LSADTKTTTVNVESKDNGKKTEVKIGAKTSVIKEKD GKLVTGKDKGENGS 300
SEQ ID 23  171 LSADTKTTTVNVESKDNGKKTEVKIGAKTSVIKEKD GKLVTGKDKGENGS 220
*****

SEQ ID 2   301 STDEGEGLVTAKEVIDAVNKAGWRMKT TTTANGQTGQADKFETV TSGTNVT 350
SEQ ID 23  221 STDEGEGLVTAKEVIDAVNKAGWRMKT TTTANGQTGQADKFETV TSGTNVT 270
*****

SEQ ID 2   351 FASGKGTTATVSKDDQGNITV MYDVNVGDALNVNQLQNSGWNLDSKAVAG 400
SEQ ID 23  271 FASGKGTTATVSKDDQGNITV MYDVNVGDALNVNQLQNSGWNLDSKAVAG 320
*****

SEQ ID 2   401 SSGKVISGNVSPSKGKMDETVINAGNNIEITRNGKNIDIATSM TPQFSS 450
SEQ ID 23  321 SSGKVISGNVSPSKGKMDETVINAGNNIEITRNGKNIDIATSM TPQFSS 370
*****

SEQ ID 2   451 VSLGAGADAP TLSVDGDALNVGSKKDNKPV RITNVAPGVKEGDVTNVAQL 500
SEQ ID 23  371 VSLGAGADAP TLSVDGDALNVGSKKDNKPV RITNVAPGVKEGDVTNVAQL 420
*****
```


df 2

SEQ ID 2 501 KGVAQNLNNRIDNVDGNARAGIAQAIATAGLVQAYLPGKSMMMAIGGGTYR 550
SEQ ID 23 421 KGVAQNLNNRIDNVDGNARAGIAQAIATAGLVQAYLPGKSMMMAIGGGTYR 470

SEQ ID 2 551 GEAGYAIGYSSISDGGNWIKGTASGNSRGHFGASASVGYQW 592
SEQ ID 23 471 GEAGYAIGYSSISDGGNWIKGTASGNSRGHFGASASVGYQW 512

of 2

```

2 Sequences Aligned      Alignment Score = 2683
Gaps Inserted = 1       Conserved Identities = 460

```

Multiple Alignment Parameters:
 Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1
 Delay Divergent = 40% Gap Distance = 8
 Similarity Matrix: id

1. SEO ID 2 vs. SEO ID 35

SEQ ID 2	1	MNKIYRIIWSALNAWVVVSELTRNHTKRASATVKTAVLATLLFATVQAS	50
SEQ ID 35	1		0

```

SEQ ID 2      51 ANNERPRKKDLYLDPVQRTVAVLIVNSDKEGTGEKEKVEENSDWAVYFNE 100
SEQ ID 35     1  NN----- 2
                **

```

```

SEQ ID 2 101 KGVLTAREITLKAGDNLKIKQNGTNFTYSLKKDLTDLTSVGTEKLSFSAN 150
SEQ ID 35 3 -----ETDLTSVGTEKLSFSAN 19
                *****

```

```

SEQ ID 2 151 GNKVNITSDTKGLNFAKETAGTNGDTTVHLNGIGSTLDTLLNTGATTNV 200
SEQ ID 35 20 GNKVNITSDTKGLNFAKETAGTNGDTTVHLNGIGSTLDTLLNTGATTNV 69
*****

```

```

SEQ ID 2 201 TNDNVTDEKKRAASVKDVLNAGWNIKGVKPGTTASDNVDFVRITYDTVEF 250
SEQ ID 35 70 TNDNVTDEKKRAASVKDVLNAGWNIKGVKPGTTASDNVDFVRITYDTVEF 119
*****

```

```

SEQ ID 2 251 LSADTKTTTVNVESKDNGKKTEVKIGAKTSVIKEKDGLVTGKDKGENS 300
SEQ ID 35 120 LSADTKTTTVNVESKDNGKKTEVKIGAKTSVIKEKDGLVTGKDKGENS 169
*****

```

```

SEQ ID 2 301 STDEGEGLVTAKEVIDAVNKAGWRMKTTTANGQTGQADKFETVTSGTNVT 350
SEQ ID 35 170 STDEGEGLVTAKEVIDAVNKAGWRMKTTTANGQTGQADKFETVTSGTNVT 219
*****

```

```

SEQ ID 2 351 FASGKGTATVSKDDQGNITVMYDVNVGDALNVNQLQNSGWNLDSKAVAG 400
SEQ ID 35 220 FASGKGTATVSKDDQGNITVMYDVNVGDALNVNQLQNSGWNLDSKAVAG 269
*****

```

```

SEQ ID 2 401 SSGKVISGNVSPSKGKMDETVNINAGNNIEITRNGKNIDIATSMTPQFSS 450
SEQ ID 35 270 SSGKVISGNVSPSKGKMDETVNINAGNNIEITRNGKNIDIATSMTPQFSS 319
*****

```

SEQ ID 2 451 VSLGAGADAPTLSDGDALNVGSKKDNKPVRLTNVAPGVKEGDVTNVAQL 500
SEQ ID 35 320 VSLGAGADAPTLSDGDALNVGSKKDNKPVRLTNVAPGVKEGDVTNVAQL 369

of 2

SEQ ID 2 501 KGVAQNLNNRIDNVDGNARAGIAQAIATAGLVQAYLPGKSMMMAIGGGTYR 550
SEQ ID 35 370 KGVAQNLNNRIDNVDGNARAGIAQAIATAGLVQAYLPGKSMMMAIGGGTYR 419

SEQ ID 2 551 GEAGYAIGYSSISDGGNWIKGTASGNSRGHFGASASVGYQW 592
SEQ ID 35 420 GEAGYAIGYSSISDGGNWIKGTASGNSRGHFGASASVGYQW 461
